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NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	JAN 02	STN pricing information for 2008 now available
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NEWS 4	JAN 28	USPATFULL, USPAT2, and USPATOLD enhanced with new custom IPC display formats
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NEWS 7	JAN 28	TOXCENTER enhanced with reloaded MEDLINE segment
NEWS 8	JAN 28	MEDLINE and LMEDLINE reloaded with enhancements
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NEWS 12	FEB 25	IMSPRODUCT reloaded with enhancements
NEWS 13	FEB 29	WPINDEX/WPIDS/WPIX enhanced with ECLA and current U.S. National Patent Classification
NEWS 14	MAR 31	IFICDB, IFIPAT, and IFIUDB enhanced with new custom IPC display formats
NEWS 15	MAR 31	CAS REGISTRY enhanced with additional experimental spectra
NEWS 16	MAR 31	CA/CAplus and CASREACT patent number format for U.S. applications updated
NEWS 17	MAR 31	LPCI now available as a replacement to LDPCI
NEWS 18	MAR 31	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS 19	APR 04	STN AnaVist, Version 1, to be discontinued
NEWS 20	APR 15	WPIDS, WPINDEX, and WPIX enhanced with new predefined hit display formats
NEWS 21	APR 28	EMBASE Controlled Term thesaurus enhanced
NEWS 22	APR 28	IMSRESEARCH reloaded with enhancements
NEWS 23	MAY 30	INPAFAMDB now available on STN for patent family searching
NEWS 24	MAY 30	DGENE, PCTGEN, and USGENE enhanced with new homology sequence search option
NEWS 25	JUN 06	EPFULL enhanced with 260,000 English abstracts
NEWS 26	JUN 06	KOREAPAT updated with 41,000 documents
NEWS 27	JUN 13	USPATFULL and USPAT2 updated with 11-character patent numbers for U.S. applications
NEWS 28	JUN 19	CAS REGISTRY includes selected substances from web-based collections
NEWS 29	JUN 25	CA/CAplus and USPAT databases updated with IPC reclassification data
NEWS 30	JUN 30	AEROSPACE enhanced with more than 1 million U.S.

FILE 'HOME' ENTERED AT 03:57:55 ON 13 JUL 2008

=> 2000DE-10034802.5
2000DE-10034802.5 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> fil capl
COST IN U.S. DOLLARS   SINCE FILE   TOTAL
                                                         ENTRY   SESSION
FULL ESTIMATED COST   0.21   0.21

FILE 'CAPLUS' ENTERED AT 03:58:20 ON 13 JUL 2008
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FILE COVERS 1907 - 13 Jul 2008 VOL 149 ISS 3
FILE LAST UPDATED: 11 Jul 2008 (20080711/ED)

Caplus now includes complete International Patent Classification (IPC)

reclassification data for the second quarter of 2008.

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They are available for your review at:

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L1            0 2000DE-10034802.5/PN

=> s DE-10034802.5/pn
L2            1 DE-10034802.5/PN
                (DE10034802/PN)

=> d ibib iabs

L2   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2002:71842  CAPLUS
DOCUMENT NUMBER:          136:123661
TITLE:                    Stable salts of o-acetylsalicylic acid with basic
                          amino acids
INVENTOR(S):              Franckowiak, Gerhard; Appolt, Hubert; Leifker, Gregor;
                          Wirges, Hans-Peter; Ledwoch, Wolfram
PATENT ASSIGNEE(S):       Bayer Aktiengesellschaft, Germany
SOURCE:                   PCT Int. Appl., 27 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 German
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 2002005782         A2    20020124    WO 2001-EP7669          20010705
     WO 2002005782         A3    20031002
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
             RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
             UZ, VN, YU, ZA, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG,
             KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR,
             IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
             GW, ML, MR, NE, SN, TD, TG
     DE 10034802           A1    20020131    DE 2000-10034802        20000718 <--
     CA 2416288            A1    20030115    CA 2001-2416288         20010705
     BR 2001012538         A     20030909    BR 2001-12538           20010705
     HU 2003002053         A2    20030929    HU 2003-2053            20010705
     EP 1365737            A2    20031203    EP 2001-956511          20010705
     EP 1365737            B1    20050420
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     JP 2004507463         T     20040311    JP 2002-511715          20010705
     AU 2001278471         B2    20040722    AU 2001-278471          20010705
     AT 293589             T     20050515    AT 2001-956511          20010705
     ES 2241849            T3    20051101    ES 2001-956511          20010705
     SK 286162             B6    20080407    SK 2003-67              20010705
     US 20020091108        A1    20020711    US 2001-906497          20010716
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US 6773724	B2	20040810			
IN 2003MN00014	A	20051021	IN 2003-MN14		20030102
NO 2003000222	A	20030116	NO 2003-222		20030116
MX 2003PA00510	A	20040420	MX 2003-PA510		20030117
ZA 2003000469	A	20040621	ZA 2003-469		20030117
KR 773658	B1	20071105	KR 2003-700713		20030117
HR 2003000108	B1	20061231	HR 2003-108		20030217
HK 1061811	A1	20060127	HK 2004-104934		20040707
US 20050009791	A1	20050113	US 2004-915652		20040809
AU 2004218728	A1	20041028	AU 2004-218728		20041013
AU 2004218728	B2	20061109			
PRIORITY APPLN. INFO.:			DE 2000-10034802	A	20000718
			AU 2001-278471	A3	20010705
			WO 2001-EP7669	W	20010705
			US 2001-906497	A3	20010716

ABSTRACT:
The invention relates to stable salts of o-acetylsalicylic acid with basic amino acids, to a method for producing them and to their use as drugs. Thus 9.9 kg acetylsalicylic acid were dissolved in 120 kg ethanol at 20-25°C; a solution of 9.0 kg lysine hydrate and 26.5 kg water were added while 30°C was not exceeded; crystallization was initiated with 50 g inoculation crystals, acetone, and cooling to 0°C. Crystals were filtered, centrifuged and dried below 40°C and 30 mbar. The yield was 89-94% ; residual moisture 0.10-0.15%.

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=>
=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	33.55	33.76

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.80	-0.80

FILE 'REGISTRY' ENTERED AT 04:31:04 ON 13 JUL 2008

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 11 JUL 2008 HIGHEST RN 1033804-48-6
DICTIONARY FILE UPDATES: 11 JUL 2008 HIGHEST RN 1033804-48-6

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on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

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=> e o-acetylsalicylic acid/cn
E1            1     O-ACETYLSALICYLALDEHYDE/CN
E2            1     O-ACETYLSALICYLAMIDE/CN
E3            1 --> O-ACETYLSALICYLIC ACID/CN
E4            1     O-ACETYLSALICYLIC ACID CHLORIDE/CN
E5            1     O-ACETYLSALICYLIC ACID TRIETHYLAMMONIUM SALT/CN
E6            1     O-ACETYLSALICYLIC ACID, Β-OXOPROPYL ESTER/CN
E7            1     O-ACETYLSALICYLIC ACID, Γ-CYANOPROPYL ESTER/CN
E8            1     O-ACETYLSALICYLOYL AZIDE/CN
E9            1     O-ACETYLSALICYLOYL CHLORIDE/CN
E10           1     O-ACETYLSALICYLOYL-D-CARNITINE/CN
E11           1     O-ACETYLSALICYLOYL-L-CARNITINE/CN
E12           1     O-ACETYLSCACONITINE/CN

=> s e3-e7
              1 "O-ACETYLSALICYLIC ACID"/CN
              1 "O-ACETYLSALICYLIC ACID CHLORIDE"/CN
              1 "O-ACETYLSALICYLIC ACID TRIETHYLAMMONIUM SALT"/CN
              1 "O-ACETYLSALICYLIC ACID, Β-OXOPROPYL ESTER"/CN
              1 "O-ACETYLSALICYLIC ACID, Γ-CYANOPROPYL ESTER"/CN
L3            5 ("O-ACETYLSALICYLIC ACID"/CN OR "O-ACETYLSALICYLIC ACID CHLORIDE
                "/CN OR "O-ACETYLSALICYLIC ACID TRIETHYLAMMONIUM SALT"/CN OR
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                SALICYLIC ACID, Γ-CYANOPROPYL ESTER"/CN)

=>     FILE MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI
COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    27.13      60.89

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)        SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00      -0.80

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=> s l3
'CN' IS NOT A VALID FIELD CODE
'CN' IS NOT A VALID FIELD CODE
'CN' IS NOT A VALID FIELD CODE
L4 184079 L3

=> s (ACETYLSALICYCLIC or 0-ACETYLSALICYCLIC) (W) ACID?
L5 1385 (ACETYLSALICYCLIC OR 0-ACETYLSALICYCLIC) (W) ACID?

=> s l5 or l4
L6 184547 L5 OR L4

=> S LYSINE OR ARGININE OR AMINOBUTYRIC OR OMITHINE or amino (W) acid
6 FILES SEARCHED...
L7 3449848 LYSINE OR ARGININE OR AMINOBUTYRIC OR OMITHINE OR AMINO (W) ACID

=> s l6 and l7
L8 4660 L6 AND L7

=> s particle (S) size or diameter or radius
L9 2087871 PARTICLE (S) SIZE OR DIAMETER OR RADIUS

=> s l8 and l9
L10 83 L8 AND L9

=> dupe rem
DUPE IS NOT A RECOGNIZED COMMAND
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"HELP COMMANDS" at an arrow prompt (=>).

=> dupe rem l10
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The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> dup rem
ENTER L# LIST OR (END):l10
PROCESSING COMPLETED FOR L10
L11 66 DUP REM L10 (17 DUPLICATES REMOVED)

=> s (ACETYLSALICYCLIC OR 0-ACETYLSALICYCLIC) (W) ACID?
L12 1385 (ACETYLSALICYCLIC OR 0-ACETYLSALICYCLIC) (W) ACID?

=> s l12 and l11
L13 0 L12 AND L11

=> d ibib iabs l11 kwic

L11 ANSWER 1 OF 66 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:674442 HCAPLUS

DOCUMENT NUMBER: 149:17763
TITLE: Nanoparticulate formulations and methods for the making and use thereof
INVENTOR(S): Shaw, Kenneth; Zhang, Mingbao
PATENT ASSIGNEE(S): Marinus Pharmaceuticals, USA
SOURCE: PCT Int. Appl., 156pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008066899	A2	20080605	WO 2007-US24606	20071128

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2006-861616P P 20061128

ABSTRACT:
The present invention is directed to size-stabilized drug nanoparticulate compns. and methods of preparation thereof. Powdered ganaxolone aqueous dispersion (1200 g) comprising a mixture of 30% ganaxolone, 5% HPMC, 0.2% sodium lauryl sulfate, and 100 ppm simethicone was milled. After 24.0 min of residence time, the ***particle*** *size* (D50) was 163 nm. Formulation of a tablet containing the nanoparticles is disclosed.

AB . . . ganaxolone, 5% HPMC, 0.2% sodium lauryl sulfate, and 100 ppm simethicone was milled. After 24.0 min of residence time, the *particle size* (D50) was 163 nm. Formulation of a tablet containing the nanoparticles is disclosed.

IT Complexing agents
Controlled-release drug delivery systems
Drug bioavailability
Particle size
Pharmaceutical capsules
Pharmaceutical nanoparticles
Pharmaceutical sprays
Pharmaceutical tablets
Stability
Stabilizing agents
(nanoparticulate formulations and methods for making and use thereof)

IT *Amino acids*, biological studies
Carboxylic acids, biological studies
Polyoxyalkylenes, biological studies
Salts, biological studies
Tocopherols
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nanoparticulate formulations and methods for making and use thereof)

IT 50-21-5D, Lactic acid, salts *50-78-2* 50-81-7, Ascorbic acid, biological studies 57-41-0, Phenytoin 65-85-0, Benzoic acid, biological studies 69-72-7, Salicylic acid, biological studies 77-92-9D, Citric acid, salts 87-66-1, Pyrogallol 87-69-4D, Tartaric acid, salts 88-27-7 89-78-1, Menthol 94-13-3, Propylparaben 98-98-6, Picolinic acid 98-98-6D, Picolinic acid, alkyl esters 99-05-8, m-Aminobenzoic acid 99-76-3, Methylparaben 100-52-7, Benzaldehyde, biological studies 104-55-2, Cinnamaldehyde 108-95-2, Phenol, biological studies 108-98-5, Thiophenol, biological studies 110-15-6D, Succinic acid, salt 110-16-7D, Maleic acid, salts 110-17-8D, Fumaric acid, salts 110-44-1, Sorbic acid 110-94-1D, Glutaric acid, salts 118-92-3, Anthranilic acid 120-80-9, Pyrocatechol, biological studies 128-37-0, biological studies 134-20-3, Methyl anthranilate 150-13-0 150-13-0D, esters 151-21-3, Sodium lauryl sulfate, biological studies 288-32-4, Imidazole, biological studies 532-32-1, Sodium benzoate 577-11-7, Docusate sodium 1948-33-0, t-Butylhydroquinone 2349-85-1 2444-28-2 5026-62-0, Sodium methylparaben 6915-15-7D, Malic acid, salts 9002-89-5, Polyvinyl alcohol 9003-39-8, Polyvinylpyrrolidone 9004-34-6, Cellulose, biological studies 9004-65-3, Hydroxypropylmethylcellulose 12619-70-4D, Cyclodextrin, inclusion complexes 25013-16-5, Butylhydroxyanisole 25322-68-3 26112-07-2, Potassium methylparaben 38398-32-2, Ganaxolone 691397-13-4, Pluronic
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nanoparticulate formulations and methods for making and use thereof)

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2 FILES SEARCHED...
'2002' NOT A VALID FIELD CODE
'2002' NOT A VALID FIELD CODE
6 FILES SEARCHED...
'2002' NOT A VALID FIELD CODE
L14 34 L11 AND (AY<=2002 OR PY<=2002)

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In a multifile environment, a format can only be used if it is valid
in at least one of the files. Refer to file specific help messages
or the STNGUIDE file for information on formats available in
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REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):d ibib iabs kwic 1-10
'D' IS NOT A VALID FORMAT
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in at least one of the files. Refer to file specific help messages
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individual files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT): ibib iabs kwic 1-10
'1-10' IS NOT A VALID FORMAT
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in at least one of the files. Refer to file specific help messages
or the STNGUIDE file for information on formats available in
individual files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):end

=> d ibib iabs kwic 1-10

L14 ANSWER 1 OF 34 MEDLINE on STN
ACCESSION NUMBER: 2001226319 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11157665
TITLE: Heterogenous nature of flow-mediated dilatation in human conduit arteries in vivo: relevance to endothelial dysfunction in hypercholesterolemia.
AUTHOR: Mullen M J; Kharbanda R K; Cross J; Donald A E; Taylor M; Vallance P; Deanfield J E; MacAllister R J
CORPORATE SOURCE: Vascular Physiology Unit, Institute of Child Health and the Centre for Clinical Pharmacology, University College London, London, UK.. MichaelJMullen@cs.com
SOURCE: Circulation research, *(2001 Feb 2)* Vol. 88, No. 2, pp. 145-51.
Journal code: 0047103. E-ISSN: 1524-4571.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 2 May 2001
Last Updated on STN: 21 May 2001
Entered Medline: 26 Apr 2001

ABSTRACT:
Flow-mediated dilatation (FMD) of conduit arteries is dependent on an intact endothelium, although the mechanisms are not fully understood. Using high-resolution ultrasound, we examined the role of endothelial mediators in radial artery dilatation in response to transient (short period of reactive hyperemia) and sustained (prolonged period of reactive hyperemia, hand warming, or an incremental infusion of acetylcholine into the distal radial artery) hyperemia. After short episodes of reactive hyperemia, FMD was abolished by local infusion of the nitric oxide synthesis inhibitor N:(G)monomethyl-L-***arginine*** (5.3+/-1.2% versus 0.7+/-0.7%, P:<0.001). In contrast, basal vessel *diameter* and dilatation after prolonged episodes of reactive hyperemia, hand warming, and distal infusion of acetylcholine were not attenuated by nitric oxide synthesis inhibition. Inhibition of cyclooxygenase or local autonomic nervous system blockade also had no effect on FMD. Patients with hypercholesterolemia exhibited reduced FMD in response to transient hyperemia, but the response to sustained hyperemia was normal. These data suggest heterogeneity of endothelial responses to blood flow that are dependent on the characteristics of the flow stimulus. Dilatation after brief episodes of hyperemia is mediated by release of nitric oxide, whereas dilatation during sustained hyperemia is unaffected by NO synthesis inhibition. Hypercholesterolemia seems to differentially affect these pathways with impairment of the nitric oxide-dependent pathway and preservation of non nitric oxide-mediated dilatation to sustained flow stimuli.
SO Circulation research, *(2001 Feb 2)* Vol. 88, No. 2, pp. 145-51.
Journal code: 0047103. E-ISSN: 1524-4571.
AB . . . artery) hyperemia. After short episodes of reactive hyperemia, FMD was abolished by local infusion of the nitric oxide synthesis inhibitor N:(G)monomethyl-L-*arginine* (5.3+/-1.2% versus 0.7+/-0.7%, P:<0.001). In contrast, basal vessel *diameter* and dilatation after prolonged episodes of reactive hyperemia, hand warming, and distal infusion of acetylcholine were not attenuated by nitric. . .
RN 10102-43-9 (Nitric Oxide); 17035-90-4 (omega-N-Methylarginine); *50-78-2 (Aspirin)*; 51-84-3 (Acetylcholine)

L14 ANSWER 2 OF 34 MEDLINE on STN
ACCESSION NUMBER: 2001100572 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11145949
TITLE: Endogenous nitric oxide and prostaglandins synergistically counteract thromboembolism in arterioles but not in venules.
AUTHOR: Broeders M A; Tangelder G J; Slaaf D W; Reneman R S; Egbrink M G
CORPORATE SOURCE: Department of Physiology, Cardiovascular Research Institute Maastricht, Maastricht University, Maastricht, the Netherlands.
SOURCE: Arteriosclerosis, thrombosis, and vascular biology, *(2001 Jan)* Vol. 21, No. 1, pp. 163-9.
Journal code: 9505803. E-ISSN: 1524-4636.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 21 May 2001
Entered Medline: 1 Feb 2001

ABSTRACT:
It has been shown that NO and prostacyclin (prostaglandin I(2)) from cultured endothelium synergistically inhibit blood platelet aggregation in vitro. However, it is unknown whether this synergism is also effective in the inhibition of thromboembolism in vivo and, if it is, whether it differs between vessel types. Therefore, the effect of endogenous NO and prostacyclin, in combination or alone, on thromboembolism was studied in an in vivo model. Thromboembolism was induced by micropipette puncture of rabbit mesenteric arterioles and venules (*diameter* 18 to 40 micrometer). In addition, the influence of wall shear rate was analyzed. In arterioles, the combined inhibition of NO synthase (N(G)-nitro-L-*arginine* [L-NA] 0.1 mmol/L; local superfusion) and of cyclooxygenase (aspirin [ASA] 100 mg/kg IV) resulted in a pronounced, significant prolongation of embolization duration (median >600 seconds) compared with control (median 153 seconds) or treatment with either L-NA (234 seconds) or ASA (314 seconds). This combined effect of L-NA+ASA was greater than the sum of the individual effects of L-NA and ASA. In contrast, in venules L-NA+ASA had no additional effect on embolization duration (209 seconds) compared with the effect of L-NA alone (230 seconds); ASA alone had no effect (122 seconds; control 72 seconds). Interestingly, only in the L-NA+ASA arterioles did embolization correlate positively with wall shear rate (r(s)=0.687; P=0.028). In conclusion, this study indicates that in arterioles, but not in venules, endogenous NO and prostaglandins synergistically counteract ongoing thromboembolism after vessel wall injury and that the combination of endogenous NO and prostaglandins appears to protect against enhancement of arteriolar thromboembolism by wall shear rate.

SO Arteriosclerosis, thrombosis, and vascular biology, *(2001 Jan)* Vol. 21, No. 1, pp. 163-9.
Journal code: 9505803. E-ISSN: 1524-4636.

AB . . . thromboembolism was studied in an in vivo model. Thromboembolism was induced by micropipette puncture of rabbit mesenteric arterioles and venules (*diameter* 18 to 40 micrometer). In addition, the influence of wall shear rate was analyzed. In arterioles, the combined inhibition of NO synthase (N(G)-nitro-L-*arginine* [L-NA] 0.1 mmol/L; local superfusion) and of cyclooxygenase (aspirin [ASA] 100 mg/kg IV) resulted in a pronounced, significant prolongation of. . .

RN 10102-43-9 (Nitric Oxide); 2149-70-4 (Nitroarginine); *50-78-2*

(Aspirin)

L14 ANSWER 3 OF 34 MEDLINE on STN
ACCESSION NUMBER: 2000028334 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10556220
TITLE: Contribution of vasodilator prostanoids and nitric oxide to resting flow, metabolic vasodilation, and flow-mediated dilation in human coronary circulation.
AUTHOR: Duffy S J; Castle S F; Harper R W; Meredith I T
CORPORATE SOURCE: Centre for Heart and Chest Research, Monash Medical Centre and Monash University, Melbourne, Australia.
SOURCE: Circulation, *(1999 Nov 9)* Vol. 100, No. 19, pp. 1951-7.
Journal code: 0147763. E-ISSN: 1524-4539.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 13 Jan 2000
Last Updated on STN: 21 May 2001
Entered Medline: 30 Nov 1999

ABSTRACT:
BACKGROUND: Endothelial dysfunction is associated with atherosclerosis and may contribute to ischemic syndromes. We assessed the contribution of endothelium-derived nitric oxide (NO) and vasodilator prostanoids to resting blood flow, metabolic vasodilation, and flow reserve in the human coronary circulation. METHODS AND RESULTS: Coronary hemodynamics were assessed before and after inhibition of vasodilator prostanoids and NO with intracoronary aspirin (acetylsalicylic acid [ASA]) and N(G)-monomethyl-L-*arginine* (L-NMMA), respectively. Angiographically smooth or mildly irregular vessels, with normal adenosine-induced coronary flow reserve, were studied in 25 patients undergoing clinically indicated procedures. Coronary blood velocity was measured by Doppler flow wire, and coronary blood flow (CBF) was calculated. ASA reduced resting conduit vessel *diameter* by 11% (P = 0.003) and CBF by 27% (P = 0.008) and increased coronary vascular resistance (CVR) by 24% (P<0.0001). ASA attenuated pacing-induced hyperemia by 28% (45.0+/-4.6 versus 32.6+/-3.4 mL/min, P = 0.005) and increased minimum CVR by 39% (2.8+/-0.3 versus 3.9+/-0.5 mm Hg x mL(-1) x min(-1), P = 0.007). L-NMMA reduced resting conduit vessel *diameter* by 9% (P = 0.05) and CBF by 20% (P = 0.08) and increased CVR by 19% (P = 0.03). L-NMMA attenuated pacing-induced hyperemia by 20% (42.4+/-5.1 versus 34.1+/-3.4 mL/min, P = 0.04) and increased minimum CVR by 33% (2.9+/-0.4 versus 3.8+/-0.5 mm Hg x mL(-1) x min(-1), P = 0.02). ASA (7.7+/-2.3% versus -1.6+/-3.2%, P = 0.06) and L-NMMA (12.1+/-3.9% versus 0.0+/-2.9%, P = 0.02) abolished pacing-induced conduit vessel flow-mediated dilation. Conclusions-Tonic release of vasodilator prostanoids and NO contributes to resting conduit and resistance vessel tone and to peak functional hyperemia and flow-mediated dilation after metabolic stimulation. This underscores the importance of normal endothelial function for metabolic vasodilation and suggests that it may be a key mechanism for preventing myocardial ischemia in coronary artery disease.
SO Circulation, *(1999 Nov 9)* Vol. 100, No. 19, pp. 1951-7.
Journal code: 0147763. E-ISSN: 1524-4539.
AB . . . Coronary hemodynamics were assessed before and after inhibition of vasodilator prostanoids and NO with intracoronary aspirin (acetylsalicylic acid [ASA]) and N(G)-monomethyl-L-*arginine* (L-NMMA), respectively. Angiographically smooth or mildly irregular vessels, with normal adenosine-induced coronary flow reserve, were studied

in 25 patients undergoing. . . blood velocity was measured by Doppler flow wire, and coronary blood flow (CBF) was calculated. ASA reduced resting conduit vessel *diameter* by 11% (P = 0.003) and CBF by 27% (P = 0.008) and increased coronary vascular resistance (CVR) by 24%. . . CVR by 39% (2.8+/-0.3 versus 3.9+/-0.5 mm Hg x mL(-1) x min(-1), P = 0.007). L-NMMA reduced resting conduit vessel *diameter* by 9% (P = 0.05) and CBF by 20% (P = 0.08) and increased CVR by 19% (P = 0.03).. . .

RN 10102-43-9 (Nitric Oxide); 17035-90-4 (omega-N-Methylarginine); *50-78-2* *(Aspirin)*; 58-61-7 (Adenosine)

L14 ANSWER 4 OF 34 MEDLINE on STN

ACCESSION NUMBER: 1998431964 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9746481
TITLE: Effect of cross-linked hemoglobin transfusion on endothelial-dependent dilation in cat pial arterioles.
AUTHOR: Asano Y; Koehler R C; Ulatowski J A; Traystman R J; Bucci E
CORPORATE SOURCE: Department of Anesthesiology/Critical Care Medicine, The Johns Hopkins University School of Medicine, Baltimore, MD 21287, USA.
CONTRACT NUMBER: HL-48517 (United States NHLBI)
SOURCE: The American journal of physiology, *(1998 Oct)* Vol. 275, No. 4 Pt 2, pp. H1313-21.
Journal code: 0370511. ISSN: 0002-9513.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 6 Jan 1999
Last Updated on STN: 6 Jan 1999
Entered Medline: 19 Nov 1998

ABSTRACT:
We determined whether addition of hemoglobin to the plasma would inhibit endothelial-dependent dilation in brain where tight endothelial junctions limit hemoglobin extravasation. Pial arteriolar *diameter* was measured by intravital microscopy through closed cranial windows in anesthetized cats either without transfusion (hematocrit = 32%) or after exchange transfusion with an albumin or sebacyl-cross-linked human hemoglobin solution (hematocrit = 18%). Dilation of small, medium, and large arterioles to acetylcholine and ADP was not significantly altered by hemoglobin transfusion. The dilatory responses were inhibited by the nitric oxide synthase inhibitor NG-nitro-L-***arginine*** , although significant dilation to 30 microM acetylcholine persisted in small arterioles in the control and albumin-transfused group but not in the hemoglobin-transfused group. The dilatory response to the nitric oxide donor 3-morpholinosydnonimine was unaffected by albumin or hemoglobin transfusion, but the response to nitroprusside was reduced by one-third after hemoglobin transfusion. When cross-linked hemoglobin was superfused through the cranial window, the acetylcholine response became inhibited at a hemoglobin concentration of 0.1 microM and was completely blocked at 10 microM. Because this concentration is substantially less than the 500 microM hemoglobin concentration in plasma after transfusion when there was no inhibition of the acetylcholine response, hemoglobin permeation of the blood-brain barrier was considered negligible. We conclude that exchange of red cell-based hemoglobin with plasma-based hemoglobin does not produce a more effective sink for endothelial-derived nitric oxide evoked by agonist receptor-mediated activation. Furthermore, decreased hematocrit does not affect agonist-evoked endothelial-dependent dilation.

SO The American journal of physiology, *(1998 Oct)* Vol. 275, No. 4 Pt 2, pp. H1313-21.
Journal code: 0370511. ISSN: 0002-9513.

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RN 2149-70-4 (Nitroarginine); 25717-80-0 (Molsidomine); 33876-97-0 (3-morpholino-sydnonimine); *50-78-2 (Aspirin)*; 51-84-3 (Acetylcholine); 74134-05-7 (bis(3,5-dibromosalicyl)sebacate)

L14 ANSWER 5 OF 34 MEDLINE on STN
ACCESSION NUMBER: 1998062938 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9400378
TITLE: Nitric oxide-independent dilation of conductance coronary arteries to acetylcholine in conscious dogs.
AUTHOR: Ming Z; Parent R; Lavallee M
CORPORATE SOURCE: Department of Physiology, Faculty of Medicine, Universite de Montreal, Quebec, Canada.
SOURCE: Circulation research, *(1997 Dec)* Vol. 81, No. 6, pp. 977-87.
Journal code: 0047103. ISSN: 0009-7330.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199712
ENTRY DATE: Entered STN: 22 Jan 1998
Last Updated on STN: 22 Jan 1998
Entered Medline: 31 Dec 1997

ABSTRACT:
NO and prostacyclin formation cannot entirely account for receptor-operated endothelium-dependent dilation of coronary vessels, since vasodilator responses are not completely suppressed by inhibitors of these agents. Therefore, we considered that another factor, such as an endothelium-derived hyperpolarizing factor described in vitro, may participate in NO- and prostacyclin-independent coronary dilator responses. In conscious instrumented dogs, intracoronary acetylcholine (ACh, 30.0 ng.kg-1.min-1) increased the external epicardial coronary *diameter* (CD) by 0.18 +/- 0.03 mm (from 3.44 +/- 0.11 mm) when increases in coronary blood flow (CBF) were prevented and increased the CD by 0.20 +/- 0.05 when CBF was allowed to increase. After the administration of intracoronary N omega-nitro-L-*arginine* methyl ester (L-NAME), CBF responses to ACh were abolished, but CD responses (0.23 +/- 0.05 from 3.22 +/- 0.09 mm) were maintained. Blockade of NO formation was confirmed by reduced CD baselines and blunted flow-dependent CD responses caused by adenosine and transient coronary artery occlusions after L-NAME administration. ACh-induced CD increases resistant to L-NAME and indomethacin were reduced after the administration of intracoronary quinacrine, an inhibitor of phospholipase A2, or proadifen, an inhibitor of cytochrome P-450. Quinacrine or proadifen alone (without L-NAME) did not alter CD responses to ACh, but L-NAME given after proadifen blunted ACh-induced increases in CD. The increases in CD caused by arachidonic acid given after L-NAME + indomethacin were antagonized by

proadifen but not altered by quinacrine. Thus, a cytochrome P-450 metabolite of arachidonic acid accounts for L-NAME-resistant and indomethacin-resistant dilation of large epicardial coronary arteries to ACh. Conversely, NO formation is the dominant mechanism of ACh-induced dilation after blockade of the cytochrome P-450 pathway.

SO Circulation research, *(1997 Dec)* Vol. 81, No. 6, pp. 977-87.
Journal code: 0047103. ISSN: 0009-7330.

AB . . . NO- and prostacyclin-independent coronary dilator responses. In conscious instrumented dogs, intracoronary acetylcholine (ACh, 30.0 ng.kg-1.min-1) increased the external epicardial coronary *diameter* (CD) by 0.18 +/- 0.03 mm (from 3.44 +/- 0.11 mm) when increases in coronary blood flow (CBF) were prevented. . . and increased the CD by 0.20 +/- 0.05 when CBF was allowed to increase. After the administration of intracoronary N omega-nitro-L-*arginine* methyl ester (L-NAME), CBF responses to ACh were abolished, but CD responses (0.23 +/- 0.05 from 3.22 +/- 0.09 mm). . .

RN 10102-43-9 (Nitric Oxide); 302-33-0 (Proadifen); *50-78-2 (Aspirin)* ; 50903-99-6 (NG-Nitroarginine Methyl Ester); 51-84-3 (Acetylcholine); 58-61-7 (Adenosine); 83-89-6 (Quinacrine)

L14 ANSWER 6 OF 34 MEDLINE on STN
ACCESSION NUMBER: 1998042169 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9374756
TITLE: Flow- and agonist-mediated nitric oxide- and prostaglandin-dependent dilation in spinal arteries.
AUTHOR: Yashiro Y; Ohhashi T
CORPORATE SOURCE: 1st Department of Physiology, Shinshu University School of Medicine, Matsumoto, Japan.
SOURCE: The American journal of physiology, *(1997 Nov)* Vol. 273, No. 5 Pt 2, pp. H2217-23.
Journal code: 0370511. ISSN: 0002-9513.
PUB. COUNTRY: United States
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199712
ENTRY DATE: Entered STN: 9 Jan 1998
Last Updated on STN: 9 Jan 1998
Entered Medline: 16 Dec 1997

ABSTRACT:
Isolated rabbit spinal resistance-sized arteries (approximately 100 microns in ***diameter*** and approximately 3 mm long) were cannulated at both ends with glass micropipettes and perfused at constant pressure (60 mmHg). An increase of flow rate corresponding to a change of pressure gradient (delta P) ranging from 0 to 20 mmHg produced a flow-dependent vasodilation. Treatment with 50 microM aspirin or 10 microM indomethacin produced a significant reduction of the flow-dependent vasodilation only at delta P of 5 mmHg. In contrast, treatment with N omega-nitro-L-*arginine* methyl ester (L-NAME, 30 microM) produced no significant change. In the presence of 10 microM indomethacin, however, 30 microM L-NAME caused a marked decrease in the arterial *diameter* at delta P of 5 mmHg, which was completely reversed with additional administration of 1 mM L-*arginine.* Acetylcholine (ACh) produced a dose-dependent increase in the arterial *diameter.* The ACh-induced vasodilation was significantly reduced by 10 microM indomethacin or 50 microM aspirin and partially suppressed by 30 microM L-NAME. Pretreatment with both indomethacin and L-NAME completely reduced the ACh-induced vasodilation. In the presence of 10 microM indomethacin,

additional treatment with 1 mM L-*arginine* significantly reversed the L-NAME-induced inhibition of the ACh-mediated vasodilation. Endothelial removal with Triton X-100 significantly reduced the ACh-induced vasodilation. Isocarbacyclin (a stable prostaglandin I2 analogue), prostaglandin E2, and arachidonic acid caused a dose-dependent dilation in the small arteries. These findings suggest that prostanoids play a major role in the flow- or ACh-induced vasodilation in the rabbit spinal resistance-sized small arteries.

SO The American journal of physiology, *(1997 Nov)* Vol. 273, No. 5 Pt 2, pp. H2217-23.
Journal code: 0370511. ISSN: 0002-9513.

AB Isolated rabbit spinal resistance-sized arteries (approximately 100 microns in *diameter* and approximately 3 mm long) were cannulated at both ends with glass micropipettes and perfused at constant pressure (60 mmHg).. . . produced a significant reduction of the flow-dependent vasodilation only at delta P of 5 mmHg. In contrast, treatment with N omega-nitro-L-*arginine* methyl ester (L-NAME, 30 microM) produced no significant change. In the presence of 10 microM indomethacin, however, 30 microM L-NAME caused a marked decrease in the arterial *diameter* at delta P of 5 mmHg, which was completely reversed with additional administration of 1 mM L-*arginine*. Acetylcholine (ACh) produced a dose-dependent increase in the arterial *diameter* . The ACh-induced vasodilation was significantly reduced by 10 microM indomethacin or 50 microM aspirin and partially suppressed by 30 microM. . . indomethacin and L-NAME completely reduced the ACh-induced vasodilation. In the presence of 10 microM indomethacin, additional treatment with 1 mM L-*arginine* significantly reversed the L-NAME-induced inhibition of the ACh-mediated vasodilation. Endothelial removal with Triton X-100 significantly reduced the ACh-induced vasodilation. Isocarbacyclin. . .

RN 10102-43-9 (Nitric Oxide); 35121-78-9 (Epoprostenol); 363-24-6 (Dinoprostone); *50-78-2 (Aspirin)*; 506-32-1 (Arachidonic Acid); 50903-99-6 (NG-Nitroarginine Methyl Ester); 51-84-3 (Acetylcholine); 53-86-1 (Indomethacin); 99946-24-4 (9-O-methanoprostaglandin I)

L14 ANSWER 7 OF 34 MEDLINE on STN
ACCESSION NUMBER: 97255979 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9101310
TITLE: Role of nitric oxide in desmopressin-induced vasodilation of microperfused rabbit afferent arterioles.
AUTHOR: Kiyomoto K; Tamaki T; Tomohiro A; Nishiyama A; Aki Y; Kimura S; Abe Y
CORPORATE SOURCE: Department of Pharmacology, Kagawa Medical School, Japan.
SOURCE: Hypertension research : official journal of the Japanese Society of Hypertension, *(1997 Mar)* Vol. 20, No. 1, pp. 29-34.
Journal code: 9307690. ISSN: 0916-9636.
PUB. COUNTRY: Japan
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 30 Jun 1997
Last Updated on STN: 30 Jun 1997
Entered Medline: 17 Jun 1997

ABSTRACT:
We have previously reported that desmopressin (dDAVP) increased the lumen ***diameter*** of norepinephrine (NE)-constricted isolated microperfused

rabbit afferent arterioles. In this study, we examined the role of nitric oxide in dDAVP-induced vasodilation of afferent arterioles. We microdissected a superficial afferent arteriole from the kidney of a New Zealand white rabbit. Each afferent arteriole was cannulated with a pipette system and microperfused in vitro at 60 mmHg. dDAVP increased the lumen *diameter* of NE-preconstricted rabbit afferent arterioles dose-dependently. dDAVP-induced vasodilation was abolished by pretreatment with NG-nitro-L-*arginine* (L-NNA, 10(-4)M) (L-NNA + NE, 6.7 +/- 1.1 microns; L-NNA + NE + dDAVP, 7.3 +/- 1.4 microns, n = 8). dDAVP increased the lumen *diameter* of NE-preconstricted afferent arterioles pretreated with L-NNA and L-***arginine*** (10(-2)M) (L-NNA + L-*arginine* + NE, 6.1 +/- 1.1 microns; L-NNA + L-*arginine* + NE + dDAVP, 8.7 +/- 0.9 microns*; *p < 0.05, n = 6). Aspirin-DL-*lysine* (10(-4)M) did not influence dDAVP-induced afferent arteriolar vasodilation (aspirin + NE, 6.4 +/- 0.8 microns; aspirin + NE + dDAVP, 9.6 +/- 1.3 microns *; *p < 0.05, n = 5). These results suggest that nitric oxide may be responsible for dDAVP-induced afferent arteriolar vasodilation.

SO Hypertension research : official journal of the Japanese Society of Hypertension, *(1997 Mar)* Vol. 20, No. 1, pp. 29-34.
Journal code: 9307690. ISSN: 0916-9636.

AB We have previously reported that desmopressin (dDAVP) increased the lumen *diameter* of norepinephrine (NE)-constricted isolated microperfused rabbit afferent arterioles. In this study, we examined the role of nitric oxide in dDAVP-induced. . . Each afferent arteriole was cannulated with a pipette system and microperfused in vitro at 60 mmHg. dDAVP increased the lumen *diameter* of NE-preconstricted rabbit afferent arterioles dose-dependently. dDAVP-induced vasodilation was abolished by pretreatment with NG-nitro-L-*arginine* (L-NNA, 10(-4)M) (L-NNA + NE, 6.7 +/- 1.1 microns; L-NNA + NE + dDAVP, 7.3 +/- 1.4 microns, n = 8). dDAVP increased the lumen *diameter* of NE-preconstricted afferent arterioles pretreated with L-NNA and L-*arginine* (10(-2)M) (L-NNA + L-*arginine* + NE, 6.1 +/- 1.1 microns; L-NNA + L-*arginine* + NE + dDAVP, 8.7 +/- 0.9 microns*; *p < 0.05, n = 6). Aspirin-DL-*lysine* (10(-4)M) did not influence dDAVP-induced afferent arteriolar vasodilation (aspirin + NE, 6.4 +/- 0.8 microns; aspirin + NE + dDAVP,. . .

CT Check Tags: Male
Animals
Arterioles: DE, drug effects
Aspirin: AA, analogs & derivatives
Aspirin: PD, pharmacology
Deamino Arginine Vasopressin: PD, pharmacology
Enzyme Inhibitors: PD, pharmacology
*Hypoglycemic Agents: PD, pharmacology
Lysine: AA, analogs & derivatives
Lysine: PD, pharmacology
NG-Nitroarginine Methyl Ester: PD, pharmacology
*Nitric Oxide: PH, physiology
Nitric Oxide Synthase: AI, antagonists & inhibitors
Norepinephrine:. . .

RN 10102-43-9 (Nitric Oxide); *16679-58-6 (Deamino Arginine Vasopressin)*; 37933-78-1 (acetylsalicylic acid lysinate); *50-78-2 (Aspirin)*; 50903-99-6 (NG-Nitroarginine Methyl Ester); 51-41-2 (Norepinephrine); *56-87-1 (Lysine)*

L14 ANSWER 8 OF 34 MEDLINE on STN
ACCESSION NUMBER: 95239949 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7723223
TITLE: Effects of angiotensin II on isolated rabbit afferent

arterioles.

AUTHOR: Yoshida H; Tamaki T; Aki Y; Kimura S; Takenaka I; Abe Y
CORPORATE SOURCE: Department of Urology, Kagawa Medical School, Japan.
SOURCE: Japanese journal of pharmacology, (1994 Dec) Vol. 66, No. 4, pp. 457-64.
Journal code: 2983305R. ISSN: 0021-5198.
PUB. COUNTRY: Japan
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199505
ENTRY DATE: Entered STN: 5 Jun 1995
Last Updated on STN: 6 Feb 1998
Entered Medline: 23 May 1995

ABSTRACT:
We examined the effects of angiotensin II (Ang II) on isolated rabbit afferent arterioles to assess the direct effect of Ang II at the resistance vessel level in the kidney. We microdissected the superficial afferent arteriole from the kidney of New Zealand White rabbits. The afferent arteriole was cannulated with a micropipette system, and the intraluminal pressure was set at 80 mmHg. Ang II did not change the lumen *diameter* of the afferent arterioles. After the afferent arterioles were pretreated with aspirin DL-*lysine* or indomethacin, Ang II (10(-7) M) caused transient vasoconstriction in the afferent arterioles. Ang II (10(-7) M) caused persistent constriction in the afferent arterioles pretreated with NG-nitro-L-*arginine* (10(-4) M). Physiological doses of Ang II decreased the lumen *diameter* of the isolated afferent arterioles pretreated with NG-nitro-L-*arginine* and aspirin DL-*lysine.* Dup753 (10(-6) M), an AT1-receptor antagonist, abolished the vasoconstrictor effects of Ang II. These findings suggest that the isolated rabbit afferent arteriole has AT1 receptors, and the vasoconstrictor response of Ang II is counteracted by vasodilatory prostaglandins and nitric oxide.

SO Japanese journal of pharmacology, (1994 Dec) Vol. 66, No. 4, pp. 457-64.
Journal code: 2983305R. ISSN: 0021-5198.

AB . . . with a micropipette system, and the intraluminal pressure was set at 80 mmHg. Ang II did not change the lumen *diameter* of the afferent arterioles. After the afferent arterioles were pretreated with aspirin DL-*lysine* or indomethacin, Ang II (10(-7) M) caused transient vasoconstriction in the afferent arterioles. Ang II (10(-7) M) caused persistent constriction in the afferent arterioles pretreated with NG-nitro-L-*arginine* (10(-4) M). Physiological doses of Ang II decreased the lumen *diameter* of the isolated afferent arterioles pretreated with NG-nitro-L-*arginine* and aspirin DL-*lysine.* Dup753 (10(-6) M), an AT1-receptor antagonist, abolished the vasoconstrictor effects of Ang II. These findings suggest that the isolated rabbit. . .

CT Check Tags: Male
Angiotensin II: AI, antagonists & inhibitors
*Angiotensin II: PD, pharmacology
Animals
Anti-Inflammatory Agents, Non-Steroidal: PD, pharmacology
Arginine: AA, analogs & derivatives
Arginine: PD, pharmacology
Arterioles: AH, anatomy & histology
Arterioles: DE, drug effects
Aspirin: AA, analogs & derivatives

Aspirin: PD, pharmacology
Biphenyl Compounds: PD, pharmacology
Imidazoles: PD, pharmacology
Indomethacin: PD, pharmacology
Losartan
Lysine: AA, analogs & derivatives
Lysine: PD, pharmacology
Nitric Oxide: AI, antagonists & inhibitors
Nitric Oxide: PD, pharmacology
Prostaglandin Antagonists: PD, pharmacology
Prostaglandins: PD, pharmacology
. . .
RN 10102-43-9 (Nitric Oxide); 11128-99-7 (Angiotensin II); 114798-26-4 (Losartan); 17035-90-4 (omega-N-Methylarginine); 37933-78-1 (acetylsalicylic acid lysinate); *50-78-2 (Aspirin)*; 53-86-1 (Indomethacin); *56-87-1 (Lysine)*; *74-79-3 (Arginine)*

L14 ANSWER 9 OF 34 MEDLINE on STN
ACCESSION NUMBER: 95171559 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7867167
TITLE: Nitric oxide is responsible for flow-dependent dilatation of human peripheral conduit arteries in vivo.
AUTHOR: Joannides R; Haefeli W E; Linder L; Richard V; Bakkali E H; Thuillez C; Luscher T F
CORPORATE SOURCE: Department of Pharmacology, Rouen University Medical School, France.
SOURCE: Circulation, *(1995 Mar 1)* Vol. 91, No. 5, pp. 1314-9.
Journal code: 0147763. ISSN: 0009-7322.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199503
ENTRY DATE: Entered STN: 7 Apr 1995
Last Updated on STN: 7 Apr 1995
Entered Medline: 24 Mar 1995
ABSTRACT:
BACKGROUND: Experimental evidence suggests that flow-dependent dilatation of conduit arteries is mediated by nitric oxide (NO) and/or prostacyclin. The present study was designed to assess whether NO or prostacyclin also contributes to flow-dependent dilatation of conduit arteries in humans. METHODS AND RESULTS: Radial artery internal *diameter* (ID) was measured continuously in 16 healthy volunteers (age, 24 +/- 1 years) with a transcutaneous A-mode echo-tracking system coupled to a Doppler device for the measurement of radial blood flow. In 8 subjects, a catheter was inserted into the brachial artery for measurement of arterial pressure and infusion of the NO synthase inhibitor NG-monomethyl-L-*arginine* (L-NMMA; 8 mumol/min for 7 minutes; infusion rate, 0.8 mL/min). Flow-dependent dilatation was evaluated before and after L-NMMA or aspirin as the response of the radial artery to an acute increase in flow (reactive hyperemia after a 3-minute cuff wrist occlusion). Under control conditions, release of the occlusion induced a marked increase in radial blood flow (from 24 +/- 3 to 73 +/- 11 mL/min; P < .01) followed by a delayed increase in radial *diameter* (flow-mediated dilatation; from 2.67 +/- 0.10 to 2.77 +/- 0.12 mm; P < .01) without any change in heart rate or arterial pressure. L-NMMA decreased basal forearm blood flow (from 24 +/- 3 to 13 +/- 3 mL/min; P < .05) without affecting basal radial artery *diameter*, heart rate, or arterial pressure, whereas aspirin (1

g PO) was without any hemodynamic effect. In the presence of L-NMMA, the peak flow response during hyperemia was not affected (76 +/- 12 mL/min), but the duration of the hyperemic response was markedly reduced, and the flow-dependent dilatation of the radial artery was abolished and converted to a vasoconstriction (from 2.62 +/- 0.11 to 2.55 +/- 0.11 mm; P < .01). In contrast, aspirin did not affect the hyperemic response nor the flow-dependent dilatation of the radial artery. CONCLUSIONS: The present investigation demonstrates that NO, but not prostacyclin, is essential for flow-mediated dilatation of large human arteries. Hence, this response can be used as a test for the L-*arginine*/NO pathway in clinical studies.

SO Circulation, *(1995 Mar 1)* Vol. 91, No. 5, pp. 1314-9.
Journal code: 0147763. ISSN: 0009-7322.

AB . . . whether NO or prostacyclin also contributes to flow-dependent dilatation of conduit arteries in humans. METHODS AND RESULTS: Radial artery internal *diameter* (ID) was measured continuously in 16 healthy volunteers (age, 24 +/- 1 years) with a transcutaneous A-mode echo-tracking system coupled. . . a catheter was inserted into the brachial artery for measurement of arterial pressure and infusion of the NO synthase inhibitor NG-monomethyl-L-*arginine* (L-NMMA; 8 mumol/min for 7 minutes; infusion rate, 0.8 mL/min). Flow-dependent dilatation was evaluated before and after L-NMMA or aspirin. . . flow (from 24 +/- 3 to 73 +/- 11 mL/min; P < .01) followed by a delayed increase in radial *diameter* (flow-mediated dilatation; from 2.67 +/- 0.10 to 2.77 +/- 0.12 mm; P < .01) without any change in heart rate. . . forearm blood flow (from 24 +/- 3 to 13 +/- 3 mL/min; P < .05) without affecting basal radial artery *diameter*, heart rate, or arterial pressure, whereas aspirin (1 g PO) was without any hemodynamic effect. In the presence of L-NMMA,. . . is essential for flow-mediated dilatation of large human arteries. Hence, this response can be used as a test for the L-*arginine*/NO pathway in clinical studies.

CT Check Tags: Female; Male
Adult
Arginine: AA, analogs & derivatives
Arginine: PD, pharmacology
Aspirin: PD, pharmacology
Blood Pressure: DE, drug effects
*Epoprostenol: PH, physiology
Forearm: BS, blood supply
Heart Rate:. . .

RN 10102-43-9 (Nitric Oxide); 17035-90-4 (omega-N-Methylarginine); 35121-78-9 (Epoprostenol); *50-78-2 (Aspirin)*; *74-79-3 (Arginine)*

L14 ANSWER 10 OF 34 MEDLINE on STN
ACCESSION NUMBER: 95142290 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7530923
TITLE: Endothelial and nonendothelial cyclooxygenase mediate rabbit pial arteriole dilation by bradykinin.
AUTHOR: Copeland J R; Willoughby K A; Tynan T M; Moore S F; Ellis E F
CORPORATE SOURCE: Department of Pharmacology and Toxicology, Medical College of Virginia, Virginia Commonwealth University, Richmond 23298-0613.
CONTRACT NUMBER: HL-42788 (United States NHLBI)
NS-07288 (United States NINDS)
NS-27214 (United States NINDS)
SOURCE: The American journal of physiology, *(1995 Jan)* Vol. 268, No. 1 Pt 2, pp. H458-66.
Journal code: 0370511. ISSN: 0002-9513.
PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199502
ENTRY DATE: Entered STN: 14 Mar 1995
Last Updated on STN: 29 Jan 1996
Entered Medline: 27 Feb 1995

ABSTRACT:
Aspirin (acetylsalicylic acid, ASA) was administered to rabbits in an attempt to inhibit selectively endothelial cyclooxygenase activity and therefore to determine its role in bradykinin-induced radical-mediated dilation of cerebral arterioles. With the use of the cranial window technique in anesthetized rabbits, pial arteriolar *diameters* were recorded in response to topically applied bradykinin, acetylcholine, and ventilation with 10% O2-9% CO2 gas mixture. Prostaglandins were measured in isolated cerebral microvessels and cerebrospinal fluid (CSF) using radioimmunoassay. Microvessel prostaglandin production was reduced significantly by 90 mg/kg i.v. ASA, whereas acetylcholine-stimulated increases of CSF prostaglandins were not similarly affected. This treatment reduced bradykinin-induced dilation of pial arterioles by 47%. After concurrent 90 mg/kg i.v. ASA plus 300 microM ASA topically applied to the brain, stimulated increases of CSF prostaglandins were reduced by 79%, while bradykinin-induced dilation was reduced by 78%. ASA did not reduce the dilator activity of either acetylcholine or ventilation with 10% O2-9% CO2. Acetylcholine- but not bradykinin-induced dilation was reduced by NG-nitro-L-*arginine* methyl ester. These results indicate intravenous ASA produced a relatively selective inhibition of cerebral microvascular cyclooxygenase and partial inhibition of bradykinin-induced dilation. Further inhibition of dilation occurred following ASA administered both systemically and topically to the brain. This indicates two sources of cyclooxygenase, endothelial and nonendothelial, mediate the bradykinin-induced dilation of rabbit pial arterioles. Furthermore, systemic doses of ASA do not eliminate brain prostaglandin formation.

SO The American journal of physiology, *(1995 Jan)* Vol. 268, No. 1 Pt 2, pp. H458-66.
Journal code: 0370511. ISSN: 0002-9513.

AB . . . in bradykinin-induced radical-mediated dilation of cerebral arterioles. With the use of the cranial window technique in anesthetized rabbits, pial arteriolar *diameters* were recorded in response to topically applied bradykinin, acetylcholine, and ventilation with 10% O2-9% CO2 gas mixture. Prostaglandins were measured. . . . the dilator activity of either acetylcholine or ventilation with 10% O2-9% CO2. Acetylcholine- but not bradykinin-induced dilation was reduced by NG-nitro-L-*arginine* methyl ester. These results indicate intravenous ASA produced a relatively selective inhibition of cerebral microvascular cyclooxygenase and partial inhibition of. . .

CT Check Tags: Male
6-Ketoprostaglandin F1 alpha: ME, metabolism
Acetylcholine: PD, pharmacology
Amino Acid Oxidoreductases: AI, antagonists & inhibitors
Animals
Arginine: AA, analogs & derivatives
Arginine: PD, pharmacology
*Arterioles: PH, physiology
Aspirin: PD, pharmacology
Blood Pressure: DE, drug effects
*Bradykinin: PD, pharmacology
*Cerebral Arteries: PH,. . .

RN 10102-43-9 (Nitric Oxide); 363-24-6 (Dinoprostone); *50-78-2*

(Aspirin); 50903-99-6 (NG-Nitroarginine Methyl Ester); 51-84-3 (Acetylcholine); 58-82-2 (Bradykinin); 58962-34-8 (6-Ketoprostaglandin F1 alpha); 74-79-3 (Arginine)
CN 0 (Cyclooxygenase Inhibitors); EC 1.14.13.39 (Nitric Oxide Synthase); EC 1.14.99.1 (Prostaglandin-Endoperoxide Synthases); EC 1.4.- (Amino Acid Oxidoreductases)

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L14 ANSWER 1 OF 34 MEDLINE on STN
ACCESSION NUMBER: 2001226319 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11157665
TITLE: Heterogenous nature of flow-mediated dilatation in human conduit arteries in vivo: relevance to endothelial dysfunction in hypercholesterolemia.
AUTHOR: Mullen M J; Kharbanda R K; Cross J; Donald A E; Taylor M; Vallance P; Deanfield J E; MacAllister R J
CORPORATE SOURCE: Vascular Physiology Unit, Institute of Child Health and the Centre for Clinical Pharmacology, University College London, London, UK.. MichaelJMullen@cs.com
SOURCE: Circulation research, (2001 Feb 2) Vol. 88, No. 2, pp. 145-51.
Journal code: 0047103. E-ISSN: 1524-4571.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 2 May 2001
Last Updated on STN: 21 May 2001
Entered Medline: 26 Apr 2001
ABSTRACT:
Flow-mediated dilatation (FMD) of conduit arteries is dependent on an intact endothelium, although the mechanisms are not fully understood. Using high-resolution ultrasound, we examined the role of endothelial mediators in radial artery dilatation in response to transient (short period of reactive hyperemia) and sustained (prolonged period of reactive hyperemia, hand warming, or an incremental infusion of acetylcholine into the distal radial artery) hyperemia. After short episodes of reactive hyperemia, FMD was abolished by local infusion of the nitric oxide synthesis inhibitor N:(G)monomethyl-L-***arginine*** (5.3+/-1.2% versus 0.7+/-0.7%, P:<0.001). In contrast, basal vessel diameter and dilatation after prolonged episodes of reactive hyperemia, hand warming, and distal infusion of acetylcholine were not attenuated by nitric oxide synthesis inhibition. Inhibition of cyclooxygenase or local autonomic nervous system blockade also had no effect on FMD. Patients with hypercholesterolemia exhibited reduced FMD in response to transient hyperemia, but the response to sustained hyperemia was normal. These data suggest heterogeneity of endothelial responses to blood flow that are dependent on the characteristics of the flow stimulus. Dilatation after brief episodes of hyperemia is mediated by release of nitric oxide, whereas dilatation during sustained hyperemia is unaffected by NO synthesis inhibition. Hypercholesterolemia seems to differentially affect these pathways with impairment of the nitric oxide-dependent pathway and preservation of non nitric oxide-mediated dilatation to sustained flow stimuli.
SO Circulation research, (2001 Feb 2) Vol. 88, No. 2, pp. 145-51.

Journal code: 0047103. E-ISSN: 1524-4571.
AB . . . artery) hyperemia. After short episodes of reactive hyperemia, FMD was abolished by local infusion of the nitric oxide synthesis inhibitor N:(G)monomethyl-L-*arginine* (5.3+/-1.2% versus 0.7+/-0.7%, P:<0.001). In contrast, basal vessel *diameter* and dilatation after prolonged episodes of reactive hyperemia, hand warming, and distal infusion of acetylcholine were not attenuated by nitric. . .
RN 10102-43-9 (Nitric Oxide); 17035-90-4 (omega-N-Methylarginine); *50-78-2* *(Aspirin)*; 51-84-3 (Acetylcholine)

L14 ANSWER 2 OF 34 MEDLINE on STN
ACCESSION NUMBER: 2001100572 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11145949
TITLE: Endogenous nitric oxide and prostaglandins synergistically counteract thromboembolism in arterioles but not in venules.
AUTHOR: Broeders M A; Tangelder G J; Slaaf D W; Reneman R S; Egbrink M G
CORPORATE SOURCE: Department of Physiology, Cardiovascular Research Institute Maastricht, Maastricht University, Maastricht, the Netherlands.
SOURCE: Arteriosclerosis, thrombosis, and vascular biology, *(2001 Jan)* Vol. 21, No. 1, pp. 163-9.
Journal code: 9505803. E-ISSN: 1524-4636.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 21 May 2001
Entered Medline: 1 Feb 2001
ABSTRACT:
It has been shown that NO and prostacyclin (prostaglandin I(2)) from cultured endothelium synergistically inhibit blood platelet aggregation in vitro. However, it is unknown whether this synergism is also effective in the inhibition of thromboembolism in vivo and, if it is, whether it differs between vessel types. Therefore, the effect of endogenous NO and prostacyclin, in combination or alone, on thromboembolism was studied in an in vivo model. Thromboembolism was induced by micropipette puncture of rabbit mesenteric arterioles and venules (*diameter* 18 to 40 micrometer). In addition, the influence of wall shear rate was analyzed. In arterioles, the combined inhibition of NO synthase (N(G)-nitro-L-*arginine* [L-NA] 0.1 mmol/L; local superfusion) and of cyclooxygenase (aspirin [ASA] 100 mg/kg IV) resulted in a pronounced, significant prolongation of embolization duration (median >600 seconds) compared with control (median 153 seconds) or treatment with either L-NA (234 seconds) or ASA (314 seconds). This combined effect of L-NA+ASA was greater than the sum of the individual effects of L-NA and ASA. In contrast, in venules L-NA+ASA had no additional effect on embolization duration (209 seconds) compared with the effect of L-NA alone (230 seconds); ASA alone had no effect (122 seconds; control 72 seconds). Interestingly, only in the L-NA+ASA arterioles did embolization correlate positively with wall shear rate (r(s)=0.687; P=0.028). In conclusion, this study indicates that in arterioles, but not in venules, endogenous NO and prostaglandins synergistically counteract ongoing thromboembolism after vessel wall injury and that the combination of endogenous NO and prostaglandins appears to protect against enhancement of arteriolar thromboembolism by wall shear rate.
SO Arteriosclerosis, thrombosis, and vascular biology, *(2001 Jan)*

Vol. 21, No. 1, pp. 163-9.
Journal code: 9505803. E-ISSN: 1524-4636.

AB . . . thromboembolism was studied in an in vivo model. Thromboembolism was induced by micropipette puncture of rabbit mesenteric arterioles and venules (*diameter* 18 to 40 micrometer). In addition, the influence of wall shear rate was analyzed. In arterioles, the combined inhibition of NO synthase (N(G)-nitro-L-*arginine* [L-NA] 0.1 mmol/L; local superfusion) and of cyclooxygenase (aspirin [ASA] 100 mg/kg IV) resulted in a pronounced, significant prolongation of. . .

RN 10102-43-9 (Nitric Oxide); 2149-70-4 (Nitroarginine); *50-78-2 (Aspirin)*

L14 ANSWER 3 OF 34 MEDLINE on STN

ACCESSION NUMBER: 2000028334 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10556220
TITLE: Contribution of vasodilator prostanoids and nitric oxide to resting flow, metabolic vasodilation, and flow-mediated dilation in human coronary circulation.
AUTHOR: Duffy S J; Castle S F; Harper R W; Meredith I T
CORPORATE SOURCE: Centre for Heart and Chest Research, Monash Medical Centre and Monash University, Melbourne, Australia.
SOURCE: Circulation, *(1999 Nov 9)* Vol. 100, No. 19, pp. 1951-7.
Journal code: 0147763. E-ISSN: 1524-4539.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 13 Jan 2000
Last Updated on STN: 21 May 2001
Entered Medline: 30 Nov 1999

ABSTRACT:
BACKGROUND: Endothelial dysfunction is associated with atherosclerosis and may contribute to ischemic syndromes. We assessed the contribution of endothelium-derived nitric oxide (NO) and vasodilator prostanoids to resting blood flow, metabolic vasodilation, and flow reserve in the human coronary circulation. METHODS AND RESULTS: Coronary hemodynamics were assessed before and after inhibition of vasodilator prostanoids and NO with intracoronary aspirin (acetylsalicylic acid [ASA]) and N(G)-monomethyl-L-*arginine* (L-NMMA), respectively. Angiographically smooth or mildly irregular vessels, with normal adenosine-induced coronary flow reserve, were studied in 25 patients undergoing clinically indicated procedures. Coronary blood velocity was measured by Doppler flow wire, and coronary blood flow (CBF) was calculated. ASA reduced resting conduit vessel *diameter* by 11% (P = 0.003) and CBF by 27% (P = 0.008) and increased coronary vascular resistance (CVR) by 24% (P<0.0001). ASA attenuated pacing-induced hyperemia by 28% (45.0+/-4.6 versus 32.6+/-3.4 mL/min, P = 0.005) and increased minimum CVR by 39% (2.8+/-0.3 versus 3.9+/-0.5 mm Hg x mL(-1) x min(-1), P = 0.007). L-NMMA reduced resting conduit vessel *diameter* by 9% (P = 0.05) and CBF by 20% (P = 0.08) and increased CVR by 19% (P = 0.03). L-NMMA attenuated pacing-induced hyperemia by 20% (42.4+/-5.1 versus 34.1+/-3.4 mL/min, P = 0.04) and increased minimum CVR by 33% (2.9+/-0.4 versus 3.8+/-0.5 mm Hg x mL(-1) x min(-1), P = 0.02). ASA (7.7+/-2.3% versus -1.6+/-3.2%, P = 0.06) and L-NMMA (12.1+/-3.9% versus 0.0+/-2.9%, P = 0.02) abolished pacing-induced conduit vessel flow-mediated dilation. Conclusions-Tonic release of vasodilator prostanoids and NO contributes to resting conduit and resistance vessel tone and to peak functional hyperemia and flow-mediated dilation after metabolic

stimulation. This underscores the importance of normal endothelial function for metabolic vasodilation and suggests that it may be a key mechanism for preventing myocardial ischemia in coronary artery disease.
SO Circulation, *(1999 Nov 9)* Vol. 100, No. 19, pp. 1951-7.
Journal code: 0147763. E-ISSN: 1524-4539.
AB . . . Coronary hemodynamics were assessed before and after inhibition of vasodilator prostanoids and NO with intracoronary aspirin (acetylsalicylic acid [ASA]) and N(G)-monomethyl-L-*arginine* (L-NMMA), respectively. Angiographically smooth or mildly irregular vessels, with normal adenosine-induced coronary flow reserve, were studied in 25 patients undergoing. . . blood velocity was measured by Doppler flow wire, and coronary blood flow (CBF) was calculated. ASA reduced resting conduit vessel *diameter* by 11% (P = 0.003) and CBF by 27% (P = 0.008) and increased coronary vascular resistance (CVR) by 24%. . . CVR by 39% (2.8+/-0.3 versus 3.9+/-0.5 mm Hg x mL(-1) x min(-1), P = 0.007). L-NMMA reduced resting conduit vessel *diameter* by 9% (P = 0.05) and CBF by 20% (P = 0.08) and increased CVR by 19% (P = 0.03).. . .
RN 10102-43-9 (Nitric Oxide); 17035-90-4 (omega-N-Methylarginine); *50-78-2 (Aspirin)*; 58-61-7 (Adenosine)

L14 ANSWER 4 OF 34 MEDLINE on STN
ACCESSION NUMBER: 1998431964 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9746481
TITLE: Effect of cross-linked hemoglobin transfusion on endothelial-dependent dilation in cat pial arterioles.
AUTHOR: Asano Y; Koehler R C; Ulatowski J A; Traystman R J; Bucci E
CORPORATE SOURCE: Department of Anesthesiology/Critical Care Medicine, The Johns Hopkins University School of Medicine, Baltimore, MD 21287, USA.
CONTRACT NUMBER: HL-48517 (United States NHLBI)
SOURCE: The American journal of physiology, *(1998 Oct)* Vol. 275, No. 4 Pt 2, pp. H1313-21.
Journal code: 0370511. ISSN: 0002-9513.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 6 Jan 1999
Last Updated on STN: 6 Jan 1999
Entered Medline: 19 Nov 1998
ABSTRACT:
We determined whether addition of hemoglobin to the plasma would inhibit endothelial-dependent dilation in brain where tight endothelial junctions limit hemoglobin extravasation. Pial arteriolar *diameter* was measured by intravital microscopy through closed cranial windows in anesthetized cats either without transfusion (hematocrit = 32%) or after exchange transfusion with an albumin or sebacyl-cross-linked human hemoglobin solution (hematocrit = 18%). Dilation of small, medium, and large arterioles to acetylcholine and ADP was not significantly altered by hemoglobin transfusion. The dilatory responses were inhibited by the nitric oxide synthase inhibitor NG-nitro-L-***arginine*** , although significant dilation to 30 microM acetylcholine persisted in small arterioles in the control and albumin-transfused group but not in the hemoglobin-transfused group. The dilatory response to the nitric oxide donor 3-morpholinosydnonimine was unaffected by albumin or hemoglobin transfusion, but the response to nitroprusside was reduced by one-third after hemoglobin transfusion. When cross-linked hemoglobin was superfused through

the cranial window, the acetylcholine response became inhibited at a hemoglobin concentration of 0.1 microM and was completely blocked at 10 microM. Because this concentration is substantially less than the 500 microM hemoglobin concentration in plasma after transfusion when there was no inhibition of the acetylcholine response, hemoglobin permeation of the blood-brain barrier was considered negligible. We conclude that exchange of red cell-based hemoglobin with plasma-based hemoglobin does not produce a more effective sink for endothelial-derived nitric oxide evoked by agonist receptor-mediated activation. Furthermore, decreased hematocrit does not affect agonist-evoked endothelial-dependent dilation.

SO The American journal of physiology, *(1998 Oct)* Vol. 275, No. 4 Pt 2, pp. H1313-21.
Journal code: 0370511. ISSN: 0002-9513.

AB . . . of hemoglobin to the plasma would inhibit endothelial-dependent dilation in brain where tight endothelial junctions limit hemoglobin extravasation. Pial arteriolar *diameter* was measured by intravital microscopy through closed cranial windows in anesthetized cats either without transfusion (hematocrit = 32%) or after. . . and ADP was not significantly altered by hemoglobin transfusion. The dilatory responses were inhibited by the nitric oxide synthase inhibitor NG-nitro-L-*arginine*, although significant dilation to 30 microM acetylcholine persisted in small arterioles in the control and albumin-transfused group but not in. . .

RN 2149-70-4 (Nitroarginine); 25717-80-0 (Molsidomine); 33876-97-0 (3-morpholino-sydnonimine); *50-78-2 (Aspirin)*; 51-84-3 (Acetylcholine); 74134-05-7 (bis(3,5-dibromosalicyl)sebacate)

L14 ANSWER 5 OF 34 MEDLINE on STN
ACCESSION NUMBER: 1998062938 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9400378
TITLE: Nitric oxide-independent dilation of conductance coronary arteries to acetylcholine in conscious dogs.
AUTHOR: Ming Z; Parent R; Lavallee M
CORPORATE SOURCE: Department of Physiology, Faculty of Medicine, Universite de Montreal, Quebec, Canada.
SOURCE: Circulation research, *(1997 Dec)* Vol. 81, No. 6, pp. 977-87.
Journal code: 0047103. ISSN: 0009-7330.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199712
ENTRY DATE: Entered STN: 22 Jan 1998
Last Updated on STN: 22 Jan 1998
Entered Medline: 31 Dec 1997

ABSTRACT:
NO and prostacyclin formation cannot entirely account for receptor-operated endothelium-dependent dilation of coronary vessels, since vasodilator responses are not completely suppressed by inhibitors of these agents. Therefore, we considered that another factor, such as an endothelium-derived hyperpolarizing factor described in vitro, may participate in NO- and prostacyclin-independent coronary dilator responses. In conscious instrumented dogs, intracoronary acetylcholine (ACh, 30.0 ng.kg-1.min-1) increased the external epicardial coronary *diameter* (CD) by 0.18 +/- 0.03 mm (from 3.44 +/- 0.11 mm) when increases in coronary blood flow (CBF) were prevented and increased the CD by 0.20 +/- 0.05 when CBF was allowed to increase. After the administration of intracoronary N omega-nitro-L-*arginine* methyl ester (L-NAME), CBF

responses to ACh were abolished, but CD responses (0.23 +/- 0.05 from 3.22 +/- 0.09 mm) were maintained. Blockade of NO formation was confirmed by reduced CD baselines and blunted flow-dependent CD responses caused by adenosine and transient coronary artery occlusions after L-NAME administration. ACh-induced CD increases resistant to L-NAME and indomethacin were reduced after the administration of intracoronary quinacrine, an inhibitor of phospholipase A2, or proadifen, an inhibitor of cytochrome P-450. Quinacrine or proadifen alone (without L-NAME) did not alter CD responses to ACh, but L-NAME given after proadifen blunted ACh-induced increases in CD. The increases in CD caused by arachidonic acid given after L-NAME + indomethacin were antagonized by proadifen but not altered by quinacrine. Thus, a cytochrome P-450 metabolite of arachidonic acid accounts for L-NAME-resistant and indomethacin-resistant dilation of large epicardial coronary arteries to ACh. Conversely, NO formation is the dominant mechanism of ACh-induced dilation after blockade of the cytochrome P-450 pathway.

SO Circulation research, *(1997 Dec)* Vol. 81, No. 6, pp. 977-87.
Journal code: 0047103. ISSN: 0009-7330.

AB . . . NO- and prostacyclin-independent coronary dilator responses. In conscious instrumented dogs, intracoronary acetylcholine (ACh, 30.0 ng.kg-1.min-1) increased the external epicardial coronary *diameter* (CD) by 0.18 +/- 0.03 mm (from 3.44 +/- 0.11 mm) when increases in coronary blood flow (CBF) were prevented. . . and increased the CD by 0.20 +/- 0.05 when CBF was allowed to increase. After the administration of intracoronary N omega-nitro-L-*arginine* methyl ester (L-NAME), CBF responses to ACh were abolished, but CD responses (0.23 +/- 0.05 from 3.22 +/- 0.09 mm). . .

RN 10102-43-9 (Nitric Oxide); 302-33-0 (Proadifen); *50-78-2 (Aspirin)* ; 50903-99-6 (NG-Nitroarginine Methyl Ester); 51-84-3 (Acetylcholine); 58-61-7 (Adenosine); 83-89-6 (Quinacrine)

L14 ANSWER 6 OF 34 MEDLINE on STN
ACCESSION NUMBER: 1998042169 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9374756
TITLE: Flow- and agonist-mediated nitric oxide- and prostaglandin-dependent dilation in spinal arteries.
AUTHOR: Yashiro Y; Ohhashi T
CORPORATE SOURCE: 1st Department of Physiology, Shinshu University School of Medicine, Matsumoto, Japan.
SOURCE: The American journal of physiology, *(1997 Nov)* Vol. 273, No. 5 Pt 2, pp. H2217-23.
Journal code: 0370511. ISSN: 0002-9513.
PUB. COUNTRY: United States
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199712
ENTRY DATE: Entered STN: 9 Jan 1998
Last Updated on STN: 9 Jan 1998
Entered Medline: 16 Dec 1997

ABSTRACT:
Isolated rabbit spinal resistance-sized arteries (approximately 100 microns in ***diameter*** and approximately 3 mm long) were cannulated at both ends with glass micropipettes and perfused at constant pressure (60 mmHg). An increase of flow rate corresponding to a change of pressure gradient (delta P) ranging from 0 to 20 mmHg produced a flow-dependent vasodilation. Treatment with 50 microM aspirin or 10 microM indomethacin produced a significant reduction of the flow-dependent vasodilation only at delta P of 5 mmHg. In contrast,

treatment with N omega-nitro-L-*arginine* methyl ester (L-NAME, 30 microM) produced no significant change. In the presence of 10 microM indomethacin, however, 30 microM L-NAME caused a marked decrease in the arterial *diameter* at delta P of 5 mmHg, which was completely reversed with additional administration of 1 mM L-*arginine.* Acetylcholine (ACh) produced a dose-dependent increase in the arterial *diameter.* The ACh-induced vasodilation was significantly reduced by 10 microM indomethacin or 50 microM aspirin and partially suppressed by 30 microM L-NAME. Pretreatment with both indomethacin and L-NAME completely reduced the ACh-induced vasodilation. In the presence of 10 microM indomethacin, additional treatment with 1 mM L-*arginine* significantly reversed the L-NAME-induced inhibition of the ACh-mediated vasodilation. Endothelial removal with Triton X-100 significantly reduced the ACh-induced vasodilation. Isocarbacyclin (a stable prostaglandin I2 analogue), prostaglandin E2, and arachidonic acid caused a dose-dependent dilation in the small arteries. These findings suggest that prostanoids play a major role in the flow- or ACh-induced vasodilation in the rabbit spinal resistance-sized small arteries.

SO The American journal of physiology, *(1997 Nov)* Vol. 273, No. 5 Pt 2, pp. H2217-23.
Journal code: 0370511. ISSN: 0002-9513.

AB Isolated rabbit spinal resistance-sized arteries (approximately 100 microns in *diameter* and approximately 3 mm long) were cannulated at both ends with glass micropipettes and perfused at constant pressure (60 mmHg).. . . produced a significant reduction of the flow-dependent vasodilation only at delta P of 5 mmHg. In contrast, treatment with N omega-nitro-L-*arginine* methyl ester (L-NAME, 30 microM) produced no significant change. In the presence of 10 microM indomethacin, however, 30 microM L-NAME caused a marked decrease in the arterial *diameter* at delta P of 5 mmHg, which was completely reversed with additional administration of 1 mM L-*arginine.* Acetylcholine (ACh) produced a dose-dependent increase in the arterial *diameter* . The ACh-induced vasodilation was significantly reduced by 10 microM indomethacin or 50 microM aspirin and partially suppressed by 30 microM. . . indomethacin and L-NAME completely reduced the ACh-induced vasodilation. In the presence of 10 microM indomethacin, additional treatment with 1 mM L-*arginine* significantly reversed the L-NAME-induced inhibition of the ACh-mediated vasodilation. Endothelial removal with Triton X-100 significantly reduced the ACh-induced vasodilation. Isocarbacyclin. . .

RN 10102-43-9 (Nitric Oxide); 35121-78-9 (Epoprostenol); 363-24-6 (Dinoprostone); *50-78-2 (Aspirin)*; 506-32-1 (Arachidonic Acid); 50903-99-6 (NG-Nitroarginine Methyl Ester); 51-84-3 (Acetylcholine); 53-86-1 (Indomethacin); 99946-24-4 (9-O-methanoprostaglandin I)

L14 ANSWER 7 OF 34 MEDLINE on STN
ACCESSION NUMBER: 97255979 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9101310
TITLE: Role of nitric oxide in desmopressin-induced vasodilation of microperfused rabbit afferent arterioles.
AUTHOR: Kiyomoto K; Tamaki T; Tomohiro A; Nishiyama A; Aki Y; Kimura S; Abe Y
CORPORATE SOURCE: Department of Pharmacology, Kagawa Medical School, Japan.
SOURCE: Hypertension research : official journal of the Japanese Society of Hypertension, *(1997 Mar)* Vol. 20, No. 1, pp. 29-34.
Journal code: 9307690. ISSN: 0916-9636.
PUB. COUNTRY: Japan
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)

(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 30 Jun 1997
Last Updated on STN: 30 Jun 1997
Entered Medline: 17 Jun 1997

ABSTRACT:
We have previously reported that desmopressin (dDAVP) increased the lumen ***diameter*** of norepinephrine (NE)-constricted isolated microperfused rabbit afferent arterioles. In this study, we examined the role of nitric oxide in dDAVP-induced vasodilation of afferent arterioles. We microdissected a superficial afferent arteriole from the kidney of a New Zealand white rabbit. Each afferent arteriole was cannulated with a pipette system and microperfused in vitro at 60 mmHg. dDAVP increased the lumen *diameter* of NE-preconstricted rabbit afferent arterioles dose-dependently. dDAVP-induced vasodilation was abolished by pretreatment with NG-nitro-L-*arginine* (L-NNA, 10(-4)M) (L-NNA + NE, 6.7 +/- 1.1 microns; L-NNA + NE + dDAVP, 7.3 +/- 1.4 microns, n = 8). dDAVP increased the lumen *diameter* of NE-preconstricted afferent arterioles pretreated with L-NNA and L-***arginine*** (10(-2)M) (L-NNA + L-*arginine* + NE, 6.1 +/- 1.1 microns; L-NNA + L-*arginine* + NE + dDAVP, 8.7 +/- 0.9 microns*; *p < 0.05, n = 6). Aspirin-DL-*lysine* (10(-4)M) did not influence dDAVP-induced afferent arteriolar vasodilation (aspirin + NE, 6.4 +/- 0.8 microns; aspirin + NE + dDAVP, 9.6 +/- 1.3 microns *; *p < 0.05, n = 5). These results suggest that nitric oxide may be responsible for dDAVP-induced afferent arteriolar vasodilation.

SO Hypertension research : official journal of the Japanese Society of Hypertension, *(1997 Mar)* Vol. 20, No. 1, pp. 29-34.
Journal code: 9307690. ISSN: 0916-9636.

AB We have previously reported that desmopressin (dDAVP) increased the lumen *diameter* of norepinephrine (NE)-constricted isolated microperfused rabbit afferent arterioles. In this study, we examined the role of nitric oxide in dDAVP-induced. . . Each afferent arteriole was cannulated with a pipette system and microperfused in vitro at 60 mmHg. dDAVP increased the lumen *diameter* of NE-preconstricted rabbit afferent arterioles dose-dependently. dDAVP-induced vasodilation was abolished by pretreatment with NG-nitro-L-*arginine* (L-NNA, 10(-4)M) (L-NNA + NE, 6.7 +/- 1.1 microns; L-NNA + NE + dDAVP, 7.3 +/- 1.4 microns, n = 8). dDAVP increased the lumen *diameter* of NE-preconstricted afferent arterioles pretreated with L-NNA and L-*arginine* (10(-2)M) (L-NNA + L-*arginine* + NE, 6.1 +/- 1.1 microns; L-NNA + L-*arginine* + NE + dDAVP, 8.7 +/- 0.9 microns*; *p < 0.05, n = 6). Aspirin-DL-*lysine* (10(-4)M) did not influence dDAVP-induced afferent arteriolar vasodilation (aspirin + NE, 6.4 +/- 0.8 microns; aspirin + NE + dDAVP,. . .

CT Check Tags: Male
Animals
Arterioles: DE, drug effects
Aspirin: AA, analogs & derivatives
Aspirin: PD, pharmacology
*Deamino Arginine Vasopressin: PD, pharmacology
Enzyme Inhibitors: PD, pharmacology
*Hypoglycemic Agents: PD, pharmacology
Lysine: AA, analogs & derivatives
Lysine: PD, pharmacology
NG-Nitroarginine Methyl Ester: PD, pharmacology
*Nitric Oxide: PH, physiology
Nitric Oxide Synthase: AI, antagonists & inhibitors

Norepinephrine:. . .
RN 10102-43-9 (Nitric Oxide); 16679-58-6 (Deamino Arginine Vasopressin); 37933-78-1 (acetylsalicylic acid lysinate); 50-78-2 (Aspirin); 50903-99-6 (NG-Nitroarginine Methyl Ester); 51-41-2 (Norepinephrine); 56-87-1 (Lysine)

L14 ANSWER 8 OF 34 MEDLINE on STN
ACCESSION NUMBER: 95239949 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7723223
TITLE: Effects of angiotensin II on isolated rabbit afferent arterioles.
AUTHOR: Yoshida H; Tamaki T; Aki Y; Kimura S; Takenaka I; Abe Y
CORPORATE SOURCE: Department of Urology, Kagawa Medical School, Japan.
SOURCE: Japanese journal of pharmacology, (1994 Dec) Vol. 66, No. 4, pp. 457-64.
Journal code: 2983305R. ISSN: 0021-5198.
PUB. COUNTRY: Japan
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199505
ENTRY DATE: Entered STN: 5 Jun 1995
Last Updated on STN: 6 Feb 1998
Entered Medline: 23 May 1995

ABSTRACT:
We examined the effects of angiotensin II (Ang II) on isolated rabbit afferent arterioles to assess the direct effect of Ang II at the resistance vessel level in the kidney. We microdissected the superficial afferent arteriole from the kidney of New Zealand White rabbits. The afferent arteriole was cannulated with a micropipette system, and the intraluminal pressure was set at 80 mmHg. Ang II did not change the lumen diameter of the afferent arterioles. After the afferent arterioles were pretreated with aspirin DL-lysine or indomethacin, Ang II (10(-7) M) caused transient vasoconstriction in the afferent arterioles. Ang II (10(-7) M) caused persistent constriction in the afferent arterioles pretreated with NG-nitro-L-arginine (10(-4) M). Physiological doses of Ang II decreased the lumen diameter of the isolated afferent arterioles pretreated with NG-nitro-L-arginine and aspirin DL-lysine. Dup753 (10(-6) M), an AT1-receptor antagonist, abolished the vasoconstrictor effects of Ang II. These findings suggest that the isolated rabbit afferent arteriole has AT1 receptors, and the vasoconstrictor response of Ang II is counteracted by vasodilatory prostaglandins and nitric oxide.
SO Japanese journal of pharmacology, (1994 Dec) Vol. 66, No. 4, pp. 457-64.
Journal code: 2983305R. ISSN: 0021-5198.
AB . . . with a micropipette system, and the intraluminal pressure was set at 80 mmHg. Ang II did not change the lumen diameter of the afferent arterioles. After the afferent arterioles were pretreated with aspirin DL-lysine or indomethacin, Ang II (10(-7) M) caused transient vasoconstriction in the afferent arterioles. Ang II (10(-7) M) caused persistent constriction in the afferent arterioles pretreated with NG-nitro-L-arginine (10(-4) M). Physiological doses of Ang II decreased the lumen diameter of the isolated afferent arterioles pretreated with NG-nitro-L-arginine and aspirin DL-lysine. Dup753 (10(-6) M), an AT1-receptor antagonist, abolished the vasoconstrictor effects of Ang II. These findings suggest that the isolated rabbit. . .

CT Check Tags: Male
Angiotensin II: AI, antagonists & inhibitors
*Angiotensin II: PD, pharmacology
Animals
Anti-Inflammatory Agents, Non-Steroidal: PD, pharmacology
Arginine: AA, analogs & derivatives
Arginine: PD, pharmacology
Arterioles: AH, anatomy & histology
Arterioles: DE, drug effects
Aspirin: AA, analogs & derivatives
Aspirin: PD, pharmacology
Biphenyl Compounds: PD, pharmacology
Imidazoles: PD, pharmacology
Indomethacin: PD, pharmacology
Losartan
Lysine: AA, analogs & derivatives
Lysine: PD, pharmacology
Nitric Oxide: AI, antagonists & inhibitors
Nitric Oxide: PD, pharmacology
Prostaglandin Antagonists: PD, pharmacology
Prostaglandins: PD, pharmacology
. . .
RN 10102-43-9 (Nitric Oxide); 11128-99-7 (Angiotensin II); 114798-26-4 (Losartan); 17035-90-4 (omega-N-Methylarginine); 37933-78-1 (acetylsalicylic acid lysinate); *50-78-2 (Aspirin)*; 53-86-1 (Indomethacin); *56-87-1 (Lysine)*; *74-79-3 (Arginine)*

L14 ANSWER 9 OF 34 MEDLINE on STN
ACCESSION NUMBER: 95171559 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7867167
TITLE: Nitric oxide is responsible for flow-dependent dilatation of human peripheral conduit arteries in vivo.
AUTHOR: Joannides R; Haefeli W E; Linder L; Richard V; Bakkali E H; Thuillez C; Luscher T F
CORPORATE SOURCE: Department of Pharmacology, Rouen University Medical School, France.
SOURCE: Circulation, *(1995 Mar 1)* Vol. 91, No. 5, pp. 1314-9.
Journal code: 0147763. ISSN: 0009-7322.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199503
ENTRY DATE: Entered STN: 7 Apr 1995
Last Updated on STN: 7 Apr 1995
Entered Medline: 24 Mar 1995

ABSTRACT:
BACKGROUND: Experimental evidence suggests that flow-dependent dilatation of conduit arteries is mediated by nitric oxide (NO) and/or prostacyclin. The present study was designed to assess whether NO or prostacyclin also contributes to flow-dependent dilatation of conduit arteries in humans.
METHODS AND RESULTS: Radial artery internal *diameter* (ID) was measured continuously in 16 healthy volunteers (age, 24 +/- 1 years) with a transcutaneous A-mode echo-tracking system coupled to a Doppler device for the measurement of radial blood flow. In 8 subjects, a catheter was inserted into the brachial artery for measurement of arterial pressure and infusion of the NO synthase inhibitor NG-monomethyl-L-*arginine* (L-NMMA; 8 mumol/min for

7 minutes; infusion rate, 0.8 mL/min). Flow-dependent dilatation was evaluated before and after L-NMMA or aspirin as the response of the radial artery to an acute increase in flow (reactive hyperemia after a 3-minute cuff wrist occlusion). Under control conditions, release of the occlusion induced a marked increase in radial blood flow (from 24 +/- 3 to 73 +/- 11 mL/min; P < .01) followed by a delayed increase in radial *diameter* (flow-mediated dilatation; from 2.67 +/- 0.10 to 2.77 +/- 0.12 mm; P < .01) without any change in heart rate or arterial pressure. L-NMMA decreased basal forearm blood flow (from 24 +/- 3 to 13 +/- 3 mL/min; P < .05) without affecting basal radial artery *diameter*, heart rate, or arterial pressure, whereas aspirin (1 g PO) was without any hemodynamic effect. In the presence of L-NMMA, the peak flow response during hyperemia was not affected (76 +/- 12 mL/min), but the duration of the hyperemic response was markedly reduced, and the flow-dependent dilatation of the radial artery was abolished and converted to a vasoconstriction (from 2.62 +/- 0.11 to 2.55 +/- 0.11 mm; P < .01). In contrast, aspirin did not affect the hyperemic response nor the flow-dependent dilatation of the radial artery. CONCLUSIONS: The present investigation demonstrates that NO, but not prostacyclin, is essential for flow-mediated dilatation of large human arteries. Hence, this response can be used as a test for the L-*arginine*/NO pathway in clinical studies.

SO Circulation, *(1995 Mar 1)* Vol. 91, No. 5, pp. 1314-9.
Journal code: 0147763. ISSN: 0009-7322.

AB . . . whether NO or prostacyclin also contributes to flow-dependent dilatation of conduit arteries in humans. METHODS AND RESULTS: Radial artery internal *diameter* (ID) was measured continuously in 16 healthy volunteers (age, 24 +/- 1 years) with a transcutaneous A-mode echo-tracking system coupled. . . a catheter was inserted into the brachial artery for measurement of arterial pressure and infusion of the NO synthase inhibitor NG-monomethyl-L-*arginine* (L-NMMA; 8 mumol/min for 7 minutes; infusion rate, 0.8 mL/min). Flow-dependent dilatation was evaluated before and after L-NMMA or aspirin. . . flow (from 24 +/- 3 to 73 +/- 11 mL/min; P < .01) followed by a delayed increase in radial *diameter* (flow-mediated dilatation; from 2.67 +/- 0.10 to 2.77 +/- 0.12 mm; P < .01) without any change in heart rate. . . forearm blood flow (from 24 +/- 3 to 13 +/- 3 mL/min; P < .05) without affecting basal radial artery *diameter*, heart rate, or arterial pressure, whereas aspirin (1 g PO) was without any hemodynamic effect. In the presence of L-NMMA,. . . is essential for flow-mediated dilatation of large human arteries. Hence, this response can be used as a test for the L-*arginine*/NO pathway in clinical studies.

CT Check Tags: Female; Male
Adult
Arginine: AA, analogs & derivatives
Arginine: PD, pharmacology
Aspirin: PD, pharmacology
Blood Pressure: DE, drug effects
*Epoprostenol: PH, physiology
Forearm: BS, blood supply
Heart Rate:. . .

RN 10102-43-9 (Nitric Oxide); 17035-90-4 (omega-N-Methylarginine); 35121-78-9 (Epoprostenol); *50-78-2 (Aspirin)*; *74-79-3 (Arginine)*

L14 ANSWER 10 OF 34 MEDLINE on STN
ACCESSION NUMBER: 95142290 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7530923
TITLE: Endothelial and nonendothelial cyclooxygenase mediate rabbit pial arteriole dilation by bradykinin.
AUTHOR: Copeland J R; Willoughby K A; Tynan T M; Moore S F; Ellis E F

CORPORATE SOURCE: Department of Pharmacology and Toxicology, Medical College of Virginia, Virginia Commonwealth University, Richmond 23298-0613.
CONTRACT NUMBER: HL-42788 (United States NHLBI)
NS-07288 (United States NINDS)
NS-27214 (United States NINDS)
SOURCE: The American journal of physiology, *(1995 Jan)* Vol. 268, No. 1 Pt 2, pp. H458-66.
Journal code: 0370511. ISSN: 0002-9513.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199502
ENTRY DATE: Entered STN: 14 Mar 1995
Last Updated on STN: 29 Jan 1996
Entered Medline: 27 Feb 1995

ABSTRACT:
Aspirin (acetylsalicylic acid, ASA) was administered to rabbits in an attempt to inhibit selectively endothelial cyclooxygenase activity and therefore to determine its role in bradykinin-induced radical-mediated dilation of cerebral arterioles. With the use of the cranial window technique in anesthetized rabbits, pial arteriolar *diameters* were recorded in response to topically applied bradykinin, acetylcholine, and ventilation with 10% O2-9% CO2 gas mixture. Prostaglandins were measured in isolated cerebral microvessels and cerebrospinal fluid (CSF) using radioimmunoassay. Microvessel prostaglandin production was reduced significantly by 90 mg/kg i.v. ASA, whereas acetylcholine-stimulated increases of CSF prostaglandins were not similarly affected. This treatment reduced bradykinin-induced dilation of pial arterioles by 47%. After concurrent 90 mg/kg i.v. ASA plus 300 microM ASA topically applied to the brain, stimulated increases of CSF prostaglandins were reduced by 79%, while bradykinin-induced dilation was reduced by 78%. ASA did not reduce the dilator activity of either acetylcholine or ventilation with 10% O2-9% CO2. Acetylcholine- but not bradykinin-induced dilation was reduced by NG-nitro-L-*arginine* methyl ester. These results indicate intravenous ASA produced a relatively selective inhibition of cerebral microvascular cyclooxygenase and partial inhibition of bradykinin-induced dilation. Further inhibition of dilation occurred following ASA administered both systemically and topically to the brain. This indicates two sources of cyclooxygenase, endothelial and nonendothelial, mediate the bradykinin-induced dilation of rabbit pial arterioles. Furthermore, systemic doses of ASA do not eliminate brain prostaglandin formation.

SO The American journal of physiology, *(1995 Jan)* Vol. 268, No. 1 Pt 2, pp. H458-66.
Journal code: 0370511. ISSN: 0002-9513.

AB . . . in bradykinin-induced radical-mediated dilation of cerebral arterioles. With the use of the cranial window technique in anesthetized rabbits, pial arteriolar *diameters* were recorded in response to topically applied bradykinin, acetylcholine, and ventilation with 10% O2-9% CO2 gas mixture. Prostaglandins were measured. . . the dilator activity of either acetylcholine or ventilation with 10% O2-9% CO2. Acetylcholine- but not bradykinin-induced dilation was reduced by NG-nitro-L-*arginine* methyl ester. These results indicate intravenous ASA produced a relatively selective inhibition of cerebral microvascular cyclooxygenase and partial inhibition of. . .

CT Check Tags: Male
6-Ketoprostaglandin F1 alpha: ME, metabolism
Acetylcholine: PD, pharmacology

*Amino Acid Oxidoreductases: AI, antagonists & inhibitors
Animals
*Arginine: AA, analogs & derivatives
Arginine: PD, pharmacology
*Arterioles: PH, physiology
Aspirin: PD, pharmacology
Blood Pressure: DE, drug effects
*Bradykinin: PD, pharmacology
*Cerebral Arteries: PH,. . .
RN 10102-43-9 (Nitric Oxide); 363-24-6 (Dinoprostone); 50-78-2 (Aspirin); 50903-99-6 (NG-Nitroarginine Methyl Ester); 51-84-3 (Acetylcholine); 58-82-2 (Bradykinin); 58962-34-8 (6-Ketoprostaglandin F1 alpha); 74-79-3 (Arginine)
CN 0 (Cyclooxygenase Inhibitors); EC 1.14.13.39 (Nitric Oxide Synthase); EC 1.14.99.1 (Prostaglandin-Endoperoxide Synthases); EC 1.4.- (Amino Acid Oxidoreductases)

=> s particle (S) (size or diameter or radius) and l14
L15 10 PARTICLE (S) (SIZE OR DIAMETER OR RADIUS) AND L14

=> d ibib iabs kwic 1-10

L15 ANSWER 1 OF 10 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2002344775 EMBASE
TITLE: Patent opportunities in matrix-based oral controlled release drug delivery systems, Part I.
AUTHOR: Gupta, Piyush; Bansal, Arvind K., Prof. (correspondence)
CORPORATE SOURCE: Dept. Pharmaceut. Technol. (Formul.), Natl. Inst. Pharmaceut. Educ./Res., Sector 67, SAS Nagar, Punjab 160 062, India. arvindb@id.eth.net
SOURCE: Pharmaceutical Technology Europe, (Sep 2002) Vol. 14, No. 9, pp. 49-50+53-54+56+58-59.
Refs: 61
ISSN: 0164-6826 CODEN: PTEUFB
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 17 Oct 2002
Last Updated on STN: 17 Oct 2002
ABSTRACT: Rapid strides have been made in the area of novel drug delivery systems (NDDSs) during the last couple of decades, which has highlighted the importance of intellectual property rights (IPRs). Recently, a large number of NDDSs have been introduced that offer a high degree of therapeutic efficacy and patient compliance, and widen the market share of dosage forms for existing drug molecules. The complexities involved in NDDS design makes IP issues of paramount importance. This article presents an overview of various possibilities and opportunities available for intellectual property protection of oral matrix-based controlled release drug delivery systems - the most popular form of NDDS.
SO Pharmaceutical Technology Europe, (Sep 2002) Vol. 14, No. 9, pp. 49-50+53-54+56+58-59.
Refs: 61

ISSN: 0164-6826 CODEN: PTEUFB

CT Medical Descriptors:
controlled . . . activity
drug blood level
*drug delivery system
drug diffusion
drug dosage form
drug efficacy
drug half life
drug industry
drug marketing
drug mixture
drug release
drug research
drug solubility
government
health care cost
human
hydrophilicity
matrix tablet
molecular weight
molecule
particle size
patent
patient compliance
review
side effect: SI, side effect
viscosity
acetylsalicylic acid: CB, drug combination
acetylsalicylic acid: PR, pharmaceutics
alginic acid: AE, adverse drug reaction
alginic acid:. . . CR, drug concentration
alginic acid: DO, drug dose
alginic acid: PO, oral drug administration
alginic acid: PR, pharmaceutics
alginic acid: PK, pharmacokinetics
alginic acid: PD, pharmacology
amino acid: CB, drug combination
amino acid: PR, pharmaceutics
aminophylline: AE, adverse drug reaction
aminophylline: CB, drug combination
aminophylline: CR, drug concentration
aminophylline: DO, drug dose
aminophylline: PO, oral drug administration
aminophylline:. . .

RN (acetylsalicylic acid) 493-53-8, *50-78-2*, 53663-74-4, 53664-49-6, 63781-77-1; (alginic acid) 28961-37-7, 29894-36-8, 9005-32-7, 9005-38-3; (*amino acid*) 65072-01-7; (aminophylline) 317-34-0; (cellulose) 61991-22-8, 68073-05-2, 9004-34-6; (dextromethorphan) 125-69-9, 125-71-3; (dihydrocodeine) 125-28-0, 24204-13-5, 5965-13-9; (gelatin) 9000-70-8; (glyceryl trinitrate) 55-63-0; (methylcellulose). . .

L15 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:77981 HCAPLUS
DOCUMENT NUMBER: 142:162662
TITLE: Nanoparticulate glipizide compositions
INVENTOR(S): Bosch, H. William; Ryde, Niels P.
PATENT ASSIGNEE(S): Elan Pharma International Limited, USA

SOURCE: U.S. Pat. Appl. Publ., 24 pp., Cont.-in-part of U.S. Ser. No. 276,400.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 18
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20050019412	A1	20050127	US 2003-701064	20031105
US 20020012675	A1	20020131	US 1999-337675	19990622 <--
WO 2001087264	A2	20011122	WO 2001-US15983	20010518 <--
WO 2001087264	A3	20020620		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 20040013613	A1	20040122	US 2003-276400	20030115

PRIORITY APPLN. INFO.:

US 1998-164351	B2	19981001
US 1999-337675	A2	19990622
WO 2001-US15983	W	20010518
US 2003-276400	A2	20030115
US 2000-572961	A	20000518

ABSTRACT:
The present invention is directed to nanoparticulate compns. comprising glipizide. The glipizide *particles* of the composition preferably have an effective average *particle size* of <2 μ. Thus, a formulation contained spray-dried glipizide 5.33, mannitol 13.47, xylitol 40.53, citric acid 19.60, sodium bicarbonate 19.33, Asparatme 0.28, PEG-4000 0.93, and sodium stearyl fumarate 0.53%.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 20050019412	A1	20050127	US 2003-701064	20031105
	US 20020012675	A1	20020131	US 1999-337675	19990622 <--
	WO 2001087264	A2	20011122	WO 2001-US15983	20010518 <--
	WO 2001087264	A3	20020620		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 20040013613	A1	20040122	US 2003-276400	20030115

AB The present invention is directed to nanoparticulate compns. comprising glipizide. The glipizide *particles* of the composition preferably have an effective average *particle size* of <2 μ. Thus, a formulation contained spray-dried glipizide 5.33, mannitol 13.47, xylitol 40.53, citric acid 19.60, sodium bicarbonate 19.33,. . .

IT Adrenoceptor agonists

Allergy
Allergy inhibitors
Anthelmintics
Anti-inflammatory agents
Antiarrhythmics
Antibacterial agents
Antibiotics
Anticoagulants
Anticonvulsants
Antidepressants
Antidiabetic agents
Antiemetics
Antihistamines
Antihypertensives
Antiobesity agents
Antitumor agents
Antitussives
Antiviral agents
Anxiety
Anxiolytics
Appetite
Appetite depressants
Blood products
Blood substitutes
Cardiovascular agents
Cardiovascular system, disease
Cholinergic agonists
Cough
Diabetes mellitus
Diagnostic agents
Dietary supplements
Dissolution
Diuretics
Dopamine agonists
Drug bioavailability
Epilepsy
Fungicides
Hemorrhage
Hemostatics
Human
Hypertension
Immunosuppressants
Inflammation
Inotropics
Muscarinic antagonists
Muscle relaxants
Mycosis
Neoplasm
Nervous system stimulants
Obesity
Particle size distribution
Radiopharmaceuticals
Stabilizing agents
Thrombosis
Vasodilators
Vomiting
α-Adrenoceptor antagonists
(nanoparticulate glipizide compns.)

IT Amine oxides

Amines, biological studies
Amino acids, biological studies
Biopolymers
Carotenes, biological studies
Caseins, biological studies
Corticosteroids, biological studies
Gelatins, biological studies
Glycerophospholipids
Lipids, biological studies
Nucleotides, biological studies
Peptides, biological studies
Phenolic resins, biological studies
Phosphates, biological studies
Phospholipids, biological studies
Phosphonium compounds
Polymers, biological studies
Polyoxyalkylenes, biological studies
Polysaccharides, biological studies
Prostaglandins
Proteins
Quaternary ammonium compounds, biological studies
Sex hormones
Sulfonium compounds
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nanoparticulate glipizide compns.)

IT 50-35-1, Thalidomide 50-44-2, Mercaptopurine 50-53-3, Chlorpromazine, biological studies *50-78-2*, Aspirin 52-53-9, Verapamil 56-81-5, Glycerol, biological studies 57-09-0, Hexadecyltrimethylammonium bromide 57-11-4, Stearic acid, biological studies 57-88-5, Cholesterol, biological studies 58-32-2, Dipyridamole 62-49-7D, Choline, esters 67-45-8, Furazolidone 69-89-6D, Xanthine, derivs. 80-74-0, Acetyl sulfisoxazole 102-71-6, Triethanolamine, biological studies 112-00-5, Lauryltrimethylammonium chloride 123-03-5, CPC 129-03-3, Cyproheptadine 132-17-2, Benztropine mesylate 139-07-1, Lauryldimethylbenzylammonium chloride 143-67-9, Vinblastine sulfate 148-79-8, Thiabendazole 151-21-3, SDS, biological studies 154-42-7, Thioguanine 303-53-7, Cyclobenzaprine 396-01-0, Triamterene 500-92-5, Proguanil 593-81-7D, Trimethylammonium chloride, coco derivs. 645-05-6, Altretamine 846-50-4, Temazepam 1119-94-4, Dodecyltrimethylammonium bromide 1119-97-7, Tetradecyltrimethylammonium bromide 1327-43-1, Magnesium aluminum silicate 1592-23-0, Calcium Stearate 1643-19-2, Tetrabutylammonium bromide 1951-25-3, Amiodarone 1977-10-2, Loxapine 2062-78-4, Pimozide 2082-84-0, Decyltrimethylammonium bromide 2498-25-1D, Dimethylhydroxyethylammonium chloride, alkyl derivs. 2609-46-3, Amiloride 2840-24-6, Trimethylammonium bromide 2840-24-6D, Trimethylammonium bromide, coco derivs. 4205-90-7, Clonidine 4342-03-4, Dacarbazine 5137-55-3, Methyltrioctylammonium chloride 5350-41-4, Benzyltrimethylammonium bromide 7173-51-5, Dimethyldidecylammonium chloride 7281-04-1, Lauryldimethylbenzylammonium bromide 9000-01-5, Gum acacia 9000-65-1, Tragacanth gum 9001-63-2, Lysozyme 9002-89-5, Poly(vinyl alcohol) 9003-39-8, Polyvinylpyrrolidone 9004-32-4, CM cellulose sodium 9004-34-6, Cellulose, biological studies 9004-54-0, Dextran, biological studies 9004-62-0, Hydroxyethyl cellulose 9004-64-2, Hydroxypropyl cellulose 9004-65-3, Hypromellose 9004-67-5, Methyl cellulose 9005-32-7, Alginate 9005-63-4D, Polyethylene glycol sorbitan, esters 9011-14-7, Poly(methyl methacrylate) 9050-04-8, CM cellulose calcium 9050-31-1, Hypromellose phthalate 10041-19-7, Dioctylsulfosuccinate 10118-90-8, Minocycline 12441-09-7D, Sorbitan, esters 13292-46-1,

Rifampin 16679-58-6, Desmopressin 16969-45-2D, Pyridinium, alkyl derivs., salts 17009-90-4D, Imidazolium, salts 18186-71-5, Dodecyltriethylammonium bromide 20526-58-3D, Sodium sulfosuccinate, alkyl esters 24280-93-1, Mycophenolic acid 25086-89-9, Vinyl acetate-vinylpyrrolidone copolymer 25301-02-4, Ethylene oxide-Formaldehyde-4-(1,1,3,3-Tetramethylbutyl)phenol copolymer 25322-68-3, Polyethylene glycol 25322-68-3D, Polyethylene glycol, alkyl ethers 26062-79-3, Poly(diallyldimethylammonium chloride) 27195-16-0, Sucrose distearate 27321-96-6, Polyethylene glycol cholesteryl ether 28228-56-0, Decyldimethylhydroxyethylammonium chloride 28679-24-5, Dodecylbenzyltriethylammonium chloride 28981-97-7, Alprazolam 29767-20-2, Teniposide 29836-26-8, n-Octyl-β-D-glucopyranoside 31431-39-7, Mebendazole 31566-31-1, Glycerol monostearate 33419-42-0, Etoposide 34911-55-2, Bupropion 36735-22-5, Quazepam 37318-31-3, Sucrose stearate 38443-60-6, Decyltriethylammonium chloride 39809-25-1, Penciclovir 42399-41-7, Diltiazem 51264-14-3, Amsacrine 52128-35-5, Trimetrexate 52467-63-7, Tricetylmethylammonium chloride 55008-57-6 55268-75-2, Cefuroxime 56422-83-4 58846-77-8, n-Decyl β-D-glucopyranoside 59080-45-4, n-Hexyl-β-D-glucopyranoside 59122-55-3, n-DoDecyl β-D-glucopyranoside 59277-89-3, Acyclovir 63722-04-3D, Dimethyl-1-naphthylmethylammonium chloride, alkyl derivs. 65271-80-9, Mitoxantrone 65277-42-1, Ketoconazole 66085-59-4, Nimodipine 67167-59-3, Polyethylene glycol stearate 69227-93-6, n-Dodecyl β-D-maltoside 69984-73-2, n-Nonyl-β-D-glucopyranoside 70458-96-7, Norfloxacin 72509-76-3, Felodipine 72558-82-8, Ceftazidime 72559-06-9, Rifabutin 73590-58-6, Omeprazole 76095-16-4, Enalapril maleate 76420-72-9, Enalaprilat 76824-35-6, Famotidine 78617-12-6, n-Heptyl-β-D-glucopyranoside 79617-96-2, Sertraline 79794-75-5, Loratadine 81098-60-4, Cisapride 81103-11-9, Clarithromycin 81409-90-7, Cabergoline 81859-24-7, Polyquat 10 82494-09-5, n-Decyl β-D-maltopyranoside 84449-90-1, Raloxifene 85261-19-4, Nonanoyl-N-methylglucamide 85261-20-7, Decanoyl-N-methylglucamide 85316-98-9, Octanoyl-N-methylglucamide 85618-20-8, β-D-Glucopyranoside, heptyl 1-thio- 85618-21-9, n-Octyl-β-D-thioglucopyranoside 85721-33-1, Ciprofloxacin 86386-73-4, Fluconazole 87679-37-6, Trandolapril 91161-71-6, Terbinafine 95233-18-4, Atovaquone 97322-87-7, Troglitazone 100286-97-3, Milrinone lactate 101397-87-9, D-Glucitol, 1-deoxy-1-[methyl(1-oxoheptyl)amino] 103577-45-3, Lansoprazole 104987-11-3, Tacrolimus 106266-06-2, Risperidone 106392-12-5, Poloxamer 110617-70-4, Poloxamine 113665-84-2, Clopidogrel 115956-12-2, Dolasetron 127377-28-0 127666-00-6 127779-20-8, Saquinavir 132539-06-1, Olanzapine 136817-59-9, Delavirdine 138402-11-6, Irbesartan 139481-59-7, Candesartan 139755-83-2, Sildenafil 144034-80-0, Rizatriptan 145599-86-6, Cerivastatin 147059-72-1, Trovafloxacin 159989-65-8, Nelfinavir mesylate 283158-20-3 329326-68-3, p-Isononylphenoxypolyglycidol 503178-50-5, Benzyl di(2-chloroethyl)ethylammonium bromide 511262-77-4D, alkyl derivs. 608094-65-1 634601-99-3, Decyldimethylhydroxyethylammonium chloride bromide 828258-69-1D, coco derivs. 828258-70-4D, coco derivs.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nanoparticulate glipizide compns.)

L15 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:352956 HCAPLUS
DOCUMENT NUMBER: 140:363037
TITLE: Formulations for topical delivery of bioactive substances and methods for their use
INVENTOR(S): Vromen, Jacob

PATENT ASSIGNEE(S): Australian Importers Ltd., USA
SOURCE: U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20040081681	A1	20040429	US 2002-281062	20021025 <--
US 7241456	B2	20070710		
CA 2543370	A1	20040513	CA 2003-2543370	20031015
WO 2004039348	A1	20040513	WO 2003-US32638	20031015
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003282834	A1	20040525	AU 2003-282834	20031015
EP 1558206	A1	20050803	EP 2003-774832	20031015
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 20070071711	A1	20070329	US 2006-535213	20060926
PRIORITY APPLN. INFO.:			US 2002-281062 A	20021025
			WO 2003-US32638 W	20031015

ABSTRACT:
The invention relates to topical delivery of bioactive agents. More particularly, the invention relates to anhydrous formulations for percutaneous absorption. The invention provides formulations that allow efficient topical delivery of high concns. of bioactive substances for percutaneous absorption. The formulations according to the invention are generally non-irritating to the skin. A preferred topical formulation comprises (1) anhydrous media containing glycerin, propylene glycol, capric/caprylic triglyceride, cetearyl alc., d-tocopherol, ascorbyl palmitate, thiodipropionic acid, BHT, phenoxyethanol, and parabens and (2) bioactive substances containing micronized niacinamide, micronized acetylsalicylic acid, and micronized ascorbic acid.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 20040081681	A1	20040429	US 2002-281062	20021025 <--
	US 7241456	B2	20070710		
	CA 2543370	A1	20040513	CA 2003-2543370	20031015
	WO 2004039348	A1	20040513	WO 2003-US32638	20031015
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FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003282834 A1 20040525 AU 2003-282834 20031015

EP 1558206 A1 20050803 EP 2003-774832 20031015

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

US 20070071711 A1 20070329 US 2006-535213 20060926

IT Acne
Anti-inflammatory agents
Antibiotics
Antimicrobial agents
Antioxidants
Antiviral agents
Athlete's foot
Burn
Chelating agents
Cosmetics
Eczema
Erythema
Fungicides
Parasiticides
Particle size
Pruritus
Psoriasis
Seborrhea
Sunscreens
Wound
(topical compns. containing delivery of micronized bioactive substances in anhydrous carriers)

IT 50-21-5, Lactic acid, biological studies 50-23-7, Hydrocortisone 50-70-4, Sorbitol, biological studies *50-78-2*, Aspirin 50-81-7, Vitamin C, biological studies 50-81-7D, Vitamin C, derivs. 51-35-4, L-Hydroxyproline 51-52-5, Propylthiouracil 51-85-4, Cystamine 52-89-1, L-Cysteine hydrochloride 52-90-4, Cysteine, biological studies 56-40-6, Glycine, biological studies 56-41-7, Alanine, biological studies 56-81-5, Glycerin, biological studies 56-81-5D, Glycerol, monoethers 56-84-8, L-Aspartic acid, biological studies 56-85-9, L-Glutamine, biological studies 56-85-9D, L-Glutamine, peptides containing 56-86-0, L-Glutamic acid, biological studies 56-86-0D, L-Glutamic acid, acyl derivs. 56-86-0D, L-Glutamic acid, derivs. 56-87-1, *Lysine*, biological studies 56-89-3, Cystine, biological studies 57-10-3, Palmitic acid, biological studies 57-55-6, Propylene glycol, biological studies 58-86-6, D-Xylose, biological studies 58-95-7, Vitamin E acetate 59-30-3, Folic acid, biological studies 59-67-6, Niacin, biological studies 60-00-4, EDTA, biological studies 60-18-4, L-Tyrosine, biological studies 60-33-3, Linoleic acid, biological studies 61-90-5, L-Leucine, biological studies 63-68-3, L-Methionine, biological studies 63-91-2, L-Phenylalanine, biological studies 64-17-5, Ethanol, biological studies 67-07-2, Creatine phosphate 67-42-5, EGTA 67-68-5, Dimethylsulfoxide, biological studies 68-19-9, Vitamin B12 69-93-2, Uric acid, biological studies 70-18-8, Glutathion, biological studies 72-18-4, L-Valine, biological studies 72-19-5, L-Threonine, biological studies 73-22-3, L-Tryptophan, biological studies 73-32-5, L-Isoleucine, biological studies 77-92-9, Citric acid, biological studies 81-25-4, Cholic acid 87-69-4D, Tartaric acid, derivs. 87-99-0, Xylitol 98-79-3, Pyroglutamic acid 103-16-2, Monobenzone 103-90-2, Acetaminophen 104-98-3, Urocanic acid 107-35-7, Taurine 107-35-7D, Taurine, derivs. 107-43-7, Trimethylglycine 110-27-0, Isopropyl myristate 110-40-7, Diethyl

sebacate 111-02-4, Squalene 111-90-0, Diethylene glycol monoethyl ether 112-80-1, Oleic acid, biological studies 118-56-9, Homosalate 118-60-5, Octyl salicylate 123-28-4 128-37-0, biological studies 131-53-3, Dioxybenzone 131-54-4, Benzophenone-6 131-55-5, Benzophenone-2 131-56-6, Benzophenone-1 131-57-7, Oxybenzone 134-09-8, Menthyl anthranilate 137-66-6, Ascorbyl palmitate 142-91-6, Isopropyl palmitate 143-28-2, Oleyl alcohol 150-13-0 153-18-4D, Rutin, glycosyl derivs. 157-07-3, Argininic acid 288-32-4D, Imidazole, derivs. 298-81-7, Methoxsalen 305-84-0, L-Carnosine 328-50-7, α-Ketoglutaric acid 372-75-8, L-Citrulline 432-70-2, α-Carotene 462-20-4, Dihydrolipoic acid 474-25-9, Chenodeoxycholic acid 500-38-9, Nordihydroguaiaretic acid 502-65-8, Lycopene 506-26-3, Gammalinolenic acid 520-36-5, Apigenin 538-23-8, Glycerin tricaprylate 541-15-1, L-Carnitine 578-74-5, Apigenin 7-O-β-glucoside 584-85-0, Anserine 588-59-0D, Stilbene, derivs. 616-91-1, N-Acetylcysteine 621-71-6, Glycerin tricaprate 645-35-2, L-Histidine hydrochloride 657-27-2, L-*Lysine* hydrochloride 693-36-7 777-11-7, Haloprogin 1119-34-2, L-*Arginine* hydrochloride 1135-24-6, Ferulic acid 1143-38-0, Anthralin 1190-63-2, Hexadecyl stearate 1314-13-2, Zinc oxide (ZnO), biological studies 1398-61-4, Chitin 1406-18-4, Vitamin E 1464-42-2, Selenomethionine 1490-04-6, Menthol 1843-05-6, Benzophenone-12 1892-31-5, Thiopropionic acid 2152-44-5, Betamethasone valerate 2491-06-7, N,N-Dimethylglycine hydrochloride 3040-38-8, Acetyl-L-carnitine 3081-61-6, L-Theanine 3184-13-2, L-Ornithine hydrochloride 3458-28-4, Mannose 4151-45-5, Cinnamate, biological studies 4159-29-9, Coniferyl benzoate 4223-03-4D, polymers with acrylate 5072-26-4 5232-99-5, Etocrylene 5306-85-4, Dimethyl isosorbide 5466-77-3, Octyl methoxycinnamate 5794-13-8, L-Asparagine monohydrate 5853-00-9, D-Carnosine 6020-87-7, Creatine monohydrate 6027-13-0D, Homocysteine, alkyl sulfoximine derivs. 6197-30-4, Octocrylene 6645-46-1, L-Carnitine hydrochloride 6915-15-7, Malic acid 6938-94-9, Diisopropyl adipate 7048-04-6, L-Cysteine hydrochloride monohydrate 7089-59-0 7235-40-7, β-Carotene 7440-66-6D, Zinc, compds. 7512-17-6, N-Acetyl-D-glucosamine 7782-49-2, Selenium, biological studies 8059-24-3, Vitamin B6 9000-92-4, Amylase 9000-99-1, Brinolase 9001-09-6, Chymopapain 9001-54-1, Hyaluronidase 9001-73-4, Papain 9001-75-6, Pepsin 9001-90-5, Plasmin 9002-01-1, Streptokinase 9002-07-7, Trypsin 9003-28-5, Polybutene 9003-39-8D, Vinylpyrrolidone polymer, alkylated derivs. 9004-07-3, Chymotrypsin 9004-61-9, Hyaluronic acid 9005-02-1, Polyethylene glycol dilaurate 9039-53-6, Urokinase 9073-60-3, Penicillinase 11103-57-4, Vitamin A 12192-57-3, Aurothioglucose 12211-28-8, Sutilains 13463-67-7, Titanium dioxide, biological studies 15687-27-1, Ibuprofen 21245-02-3, Padimate O 22393-86-8, Cetyl oleate 22839-47-0, Aspartame 23513-68-0 23513-69-1 23593-75-1, Clotrimazole 25013-16-5, Butylhydroxyanisole 25086-89-9, Vinylpyrrolidone-vinylacetate copolymer 25155-18-4, Methylbenzethonium chloride 26942-95-0 33564-31-7, Diflorasone diacetate 34466-20-1, DL-Ribose 36653-82-4, Hexadecyl alcohol 36687-82-8, biological studies 36861-47-9 37259-58-8, Serine protease 37341-53-0, Keratinase 51022-69-6, Amcinonide 51667-26-6D, Oxazolidinone, derivs. 52262-23-4, Trihydroxybutyrophenone 56265-06-6 57828-26-9, Lipoic acid 59277-89-3, 9-[(2-Hydroxyethoxy)methyl]guanine 64364-41-6 64872-77-1, Butoconazole nitrate 64911-86-0, Formaldehyde-ditolyl ether sulfonic acid 66734-13-2, Alclometasone dipropionate 70356-09-1, Butylmethoxydibenzoylmethane 76606-83-2 82204-86-2 92414-48-7 98487-37-7 104443-75-6 108333-82-0, D,L-Carnosine 108910-78-7, Magnesium ascorbyl phosphate 113284-00-7, Ethyl 4-[bis(hydroxypropyl)]aminobenzoate 135326-54-4, Propylene glycol

myristyl ether acetate 143549-76-2, L-Ascorbyl acetate 150977-36-9, Bromelain 162041-44-3, biological studies 208535-04-0, Creatine pyruvate 220349-64-4, L-Carnitine fumarate, biological studies 681806-79-1
RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(topical compns. containing delivery of micronized bioactive substances in anhydrous carriers)

L15 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:657934 HCAPLUS
DOCUMENT NUMBER: 137:206536
TITLE: Cubic liquid crystalline compositions and methods for their preparation
INVENTOR(S): Spicer, Patrick Thomas; Small, William Broderick, II; Lynch, Matthew Lawrence
PATENT ASSIGNEE(S): The Procter & Gamble Company, USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002066014	A2	20020829	WO 2002-US4776		20020219 <--
WO 2002066014	A3	20030904			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 20020160040	A1	20021031	US 2001-990552		20011121 <--
US 7008646	B2	20060307			
CA 2434647	A1	20020829	CA 2002-2434647		20020219 <--
AU 2002251986	A1	20020904	AU 2002-251986		20020219 <--
AU 2002251986	B2	20061221			
EP 1361865	A2	20031119	EP 2002-721031		20020219 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004521125	T	20040715	JP 2002-565574		20020219 <--
CN 1638735	A	20050713	CN 2002-805147		20020219 <--
MX 2003PA07440	A	20031204	MX 2003-PA7440		20030820
PRIORITY APPLN. INFO.:			US 2001-269953P	P	20010220
			US 2001-990552	A	20011121
			WO 2002-US4776	W	20020219

ABSTRACT:
A dry powder cubic gel precursor comprising an encapsulating compound, an amphiphile capable of forming a cubic liquid crystalline phase, and optionally a solvent is described. The encapsulating compound (A), amphiphile (B), and optional solvent (C) are present in mass fractions relative to each other such that 1.0 = a + b + c, wherein a is the mass fraction of A, b is the mass fraction of B, and c is the mass fraction of C. Further, 1.0 > a > 0, 1.0 > b

> 0, 1.0 > c > 0 and a, b, and c do not fall within a cubic liquid crystalline phase region on a phase diagram representing phase behavior of A, B, and C. A method of making the cubic gel precursor comprises the steps of: (i) dissolving an encapsulating compound in a solvent; (ii) adding an amphiphile; (iii) mixing the encapsulating compound and amphiphile, wherein steps (i), (ii), and (iii) are performed in any order; (iv) atomizing the mixture obtained; and, (v) drying the mixture For example, an active ingredient (fatty acid solution) was encapsulated in powders made by spray-drying a liquid solution The liquid solution was prepared from a
premix of 67% water and 33% starch at 70°. A second solution of 90% monoolein and 10% fatty acid mix (20% omega-3, 80% triglyceride oil) was prepared at 60°. The oil solution was then added to the starch-water solution forming a 9% monoolein, 30% starch, 60% water, and 1% fatty acid mixture A high shear mixing system was used to keep the system mixed and maintained above 90°. The mixture was then pumped at a rate of 8 mL/min through the liquid side of a twin-fluid atomizer, with slight adjustments being made to the flow rate to keep the temperature of the exit air in the system between 90-100°. The liquid feed was atomized with air at a pressure of 42.6 psi (293.5 kPa). Upon drying, the powder has a composition of 22.5% monoolein, 75% starch, and 2.5% fatty acid mixture The powder appears to exhibit a bimodal *size* distribution of larger 10 μm *particles* and smaller 3-5 μm ***particles*** , all of which exhibit the classical shrinkage that is characteristic of starch capsules during their cooling. The uniform appearance of the powders can be an excellent indicator that the fatty acid active is encapsulated within the starch shells.

PI WO 2002066014 A2 *20020829*

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI WO 2002066014	A2	20020829	WO 2002-US4776	20020219	<--
WO 2002066014	A3	20030904			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 20020160040	A1	20021031	US 2001-990552	20011121	<--
US 7008646	B2	20060307			
CA 2434647	A1	20020829	CA 2002-2434647	20020219	<--
AU 2002251986	A1	20020904	AU 2002-251986	20020219	<--
AU 2002251986	B2	20061221			
EP 1361865	A2	20031119	EP 2002-721031	20020219	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004521125	T	20040715	JP 2002-565574	20020219	<--
CN 1638735	A	20050713	CN 2002-805147	20020219	<--
MX 2003PA07440	A	20031204	MX 2003-PA7440	20030820	

AB . . . has a composition of 22.5% monoolein, 75% starch, and 2.5% fatty acid mixture The powder appears to exhibit a bimodal *size* distribution of larger 10 μm *particles* and smaller 3-5 μm *particles*, all of which exhibit the classical shrinkage that is characteristic of starch capsules during their cooling. The uniform appearance of. . .

IT *Amino acids*, biological studies

Essential oils
Fatty acids, biological studies
Glycols, biological studies
Monoglycerides
Monosaccharides
Polyoxyalkylenes, biological studies
Polysaccharides, biological studies
Proteins
Vitamins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of powders as precursors of cubic liquid crystalline gel particles)

IT 50-23-7, Hydrocortisone *50-78-2*, Acetylsalicylic acid 51-05-8, Procaine hydrochloride 54-21-7, Sodium salicylate 55-22-1, Isonicotinic acid, biological studies 55-63-0, Nitroglycerin 56-81-5, Glycerol, biological studies 57-55-6, Propylene glycol, biological studies 58-08-2, Caffeine, biological studies 60-33-3D, Linoleic acid, derivs. 61-33-6, Benzyl penicillin, biological studies 64-75-5, Tetracycline hydrochloride 67-68-5, Dimethyl sulfoxide, biological studies 73-31-4, Melatonin 73-78-9, Lidocaine hydrochloride 75-12-7D, Formamide, derivs. 87-66-1, Pyrogallol 93-14-1, Guaifenesin 98-92-0, Nicotinamide 107-21-1, Ethylene glycol, biological studies 108-46-3, Resorcinol, biological studies 111-62-6, Ethyl oleate 156-54-7, Sodium butyrate 299-42-3, Ephedrine 345-78-8, Pseudoephedrine hydrochloride 443-48-1, Metronidazole 515-42-4, Sodium benzene sulfonate 532-32-1, Sodium benzoate 538-42-1, Sodium cinnamate 657-84-1, Sodium toluene sulfonate 721-50-6, Prilocaine 1300-72-7, Sodium xylene sulfonate 1406-18-4, Vitamin E 5015-75-8, Sodium p-bromobenzene sulfonate 6284-40-8D, N-Methylglucamine, alkoxycarbonyl derivs. 9003-11-6, Ethylene oxide-propylene oxide copolymer 9004-10-8, Insulin, biological studies 9004-54-0, Dextran, biological studies 9005-25-8, Starch, biological studies 12441-09-7D, Sorbitan, derivs. 12619-70-4, Cyclodextrin 13463-41-7, Zinc pyrithione 14206-62-3 14838-15-4, Phenylpropanolamine 16887-79-9 22071-15-4, Ketoprofen 22113-86-6, Ethylammonium nitrate 22669-27-8, p-Aminobenzoic acid hydrochloride 23593-75-1, Clotrimazole 25322-68-3, Polyethylene glycol 25496-72-4, Glycerol monooleate 25618-55-7D, Polyglycerol, esters 26545-74-4, Monolinolein 26921-17-5, Timolol maleate 27137-20-8, Sodium benzene disulfonate 28348-53-0, Sodium cumene sulfonate 31566-31-1, Glycerol monostearate 38304-91-5, Minoxidil 59277-89-3, Acyclovir 68278-23-9, Eflornithine hydrochloride 74563-64-7 106392-12-5, Poloxamer 407 171599-83-0, Sildenafil citrate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of powders as precursors of cubic liquid crystalline gel particles)

L15 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:555334 HCAPLUS
DOCUMENT NUMBER: 137:114525
TITLE: Syntactic deformable pharmaceutical foam compositions
INVENTOR(S): Odidi, Isa; Odidi, Amina
PATENT ASSIGNEE(S): Can.
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002056861	A2	20020725	WO 2002-CA54	20020117 <--
WO 2002056861	A3	20021017		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 6800668	B1	20041005	US 2001-765783	20010119 <--
CA 2435276	A1	20020725	CA 2002-2435276	20020117 <--
CA 2435276	C	20050315		
AU 2002226223	A1	20020730	AU 2002-226223	20020117 <--
PRIORITY APPLN. INFO.:			US 2001-765783 A	20010119
			WO 2002-CA54 W	20020117

ABSTRACT:
The invention relates to methods for preparing a syntactic foam composition suitable for use as a carrier for chems. or other compds., including pharmaceuticals. Carbopol 971P, hydroxyethyl cellulose, cellulose microspheres and silica, was mixed in a high-shear mixer. The resulting admixt. was treated with 2-propanol, while simultaneously subjecting the admixt. to high-shear forces in the high-shear mixer. This mixing created a uniform stable syntactic deformable and compressible dendritic solid foam which could be shaped before drying. Metoprolol succinate was added to the above admixt. and subjected to high-shear agitation for 2 min before treatment with 2-propanol. A stable syntactic deformable and compressible dendritic solid foam which could be shaped before drying was obtained. This was dried at 40°. The dried foam was the disentangled by *size* reduction to obtain discrete ***particles.*** The free flowing particles were reassembled and shaped by compression in a mold. The shaped units, when subjected to an aqueous medium, released metoprolol over a period of ≤3 h.

PI WO 2002056861 A2 *20020725*

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002056861	A2	20020725	WO 2002-CA54	20020117 <--
WO 2002056861	A3	20021017		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 6800668	B1	20041005	US 2001-765783	20010119 <--
CA 2435276	A1	20020725	CA 2002-2435276	20020117 <--
CA 2435276	C	20050315		
AU 2002226223	A1	20020730	AU 2002-226223	20020117 <--

AB . . . which could be shaped before drying was obtained. This was dried at 40°. The dried foam was the disentangled by *size* reduction to obtain discrete *particles.* The free flowing particles were reassembled and shaped by compression in a mold. The shaped units, when subjected to an. . .

IT 50-02-2, Dexamethasone 50-28-2, Estradiol, biological studies 50-48-6, Amitriptyline 50-70-4, Sorbitol, biological studies *50-78-2*, Aspirin 50-99-7, Glucose, biological studies 51-48-9, Levothyroxine, biological studies 53-03-2, Prednisone 54-31-9, Furosemide 57-27-2, Morphine, biological studies 57-41-0, Phenytoin 57-50-1, Sucrose, biological studies 57-63-6, EthinylEstradiol 58-93-5, Hydrochlorothiazide 59-92-7, Levodopa, biological studies 60-87-7, Promethazine 63-42-3, Lactose 67-20-9, Nitrofurantoin 68-22-4, Norethindrone 69-65-8, Mannitol 76-42-6, Oxycodone 76-57-3, Codeine 78-44-4, Carisoprodol 81-81-2, Warfarin 83-43-2, Methylprednisolone 87-99-0, Xylitol 89-57-6, Mesalamine 90-82-4, Pseudoephedrine 93-14-1, Guaifenesin 99-66-1, Pentanoic acid, 2-propyl 103-90-2, Acetaminophen 114-07-8, Erythromycin 125-29-1, Hydrocodone 127-07-1, Hydroxyurea 132-98-9, Penicillin VK 155-09-9, Tranylcypromine 300-62-9D, Amphetamine, salts 303-53-7, Cyclobenzaprine 315-30-0, Allopurinol 378-44-9, Betamethasone 396-01-0, Triamterene 439-14-5, Diazepam 469-62-5, Propoxyphene 525-66-6, Propranolol 673-06-3, D-Phenylalanine 797-63-7, Levonorgestrel 846-49-1, Lorazepam 846-50-4, Temazepam 1119-34-2, L-*Arginine* hydrochloride 1622-61-3, Clonazepam 3056-17-5, Stavudine 3930-20-9, Sotalol 4205-90-7, Clonidine 4419-39-0, Beclomethasone 7447-40-7, Potassium Chloride, biological studies 7460-12-0, Pseudoephedrine sulfate 7481-89-2, Zalcitabine 7631-86-9, Silica, biological studies 9002-89-5, Polyvinyl alcohol 9002-96-4, α-Tocopherol polyethylene glycol succinate 9003-39-8, Povidone 9004-34-6, Cellulose, biological studies 9004-54-0, Dextran, biological studies 9004-62-0, Hydroxyethyl Cellulose 9004-65-3, Hydroxypropyl Methyl cellulose 9005-25-8, Starch, biological studies 9007-12-9, Calcitonin 10238-21-8, Glyburide 10540-29-1, Tamoxifen 11138-66-2, Xanthan gum 12650-69-0, Mupirocin 15686-71-2, Cephalexin 15687-27-1, Ibuprofen 16051-77-7, Isosorbide Mononitrate 18559-94-9, Albuterol 18641-57-1, Glyceryl behenate 19794-93-5, Trazodone 20830-75-5, Digoxin 21256-18-8, Oxaprozin 22204-53-1, Naproxen 23593-75-1, Clotrimazole 24980-41-4, Poly(ε-caprolactone) 25086-15-1, Eudragit L100 25248-42-4, Poly[oxy(1-oxo-1,6-hexanediyl)] 25322-68-3, Polyethylene glycol 25812-30-0, Gemfibrozil 26009-03-0, Poly(glycolic acid) 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6, Poly(lactic acid) 26124-68-5, Poly(glycolic acid) 26787-78-0, Amoxicillin 28860-95-9, Carbidopa 28981-97-7, Alprazolam 29122-68-7, Atenolol 30516-87-1, Zidovudine 32986-56-4, Tobramycin 34346-01-5, Glycolic acid-lactic acid copolymer 51384-51-1, Metoprolol 54739-18-3, Fluvoxamine 54910-89-3, Fluoxetine 55268-75-2, Cefuroxime 56180-94-0, Acarbose 58001-44-8 59122-46-2, Misoprostol 59729-33-8, Citalopram 59803-98-4, Brimonidine 60205-81-4, Ipratropium 61869-08-7, Paroxetine 63590-64-7, Terazosin 63675-72-9, Nisoldipine 66357-35-5, Ranitidine 66376-36-1, Alendronate 66722-44-9, Bisoprolol 69655-05-6, Didanosine 72432-03-2, Miglitol 72509-76-3, Felodipine 72956-09-3, Carvedilol 74191-85-8, Doxazosin 75330-75-5, Lovastatin 75847-73-3, Enalapril 76547-98-3, Lisinopril 76584-70-8, Divalproex sodium 76824-35-6, Famotidine 76963-41-2, Nizatidine 78644-42-5, Poly(malic acid) 78666-19-0, Poly(malic acid), SRU 79617-96-2, Sertraline 79794-75-5, Loratadine 79902-63-9, Simvastatin 80474-14-2, Fluticasone Propionate 81093-37-0, Pravastatin 81098-60-4, Cisapride 81103-11-9, Clarithromycin 82419-36-1, Ofloxacin 82626-48-0, Zolpidem 83799-24-0, Fexofenadine 83881-51-0, Cetirizine 83905-01-5, Azithromycin 84449-90-1, Raloxifene 85441-61-8, Quinapril 85721-33-1, Ciprofloxacin 86541-75-5, Benazepril 87333-19-5, Ramipril 88150-42-9, Amlodipine 89365-50-4, Salmeterol 91161-71-6, Terbinafine 92665-29-7, Cefprozil 93413-69-5, Venlafaxine 93479-97-1, Glimepiride

93957-54-1, Fluvastatin 97322-87-7, Troglitazone 98048-97-6, Fosinopril 98418-47-4, Metoprolol succinate 99614-02-5, Ondansetron 100986-85-4, Levofloxacin 103577-45-3, Lansoprazole 103628-46-2, Sumatriptan 104632-26-0, Pramipexole 105102-22-5, Mometasone 106133-20-4, Tamsulosin 106266-06-2, Risperidone 107753-78-6, Zafirlukast 109889-09-0, Granisetron 111974-69-7, Quetiapine 113665-84-2, Clopidogrel 114798-26-4, Losartan 120014-06-4, Donepezil 124937-51-5, Tolterodine 127779-20-8, Saquinavir 129618-40-2, Nevirapine 130209-82-4, Latanoprost 132539-06-1, Olanzapine 134523-00-5, Atorvastatin 134678-17-4, Lamivudine 135062-02-1, Repaglinide 136470-78-5, Abacavir 136817-59-9, Delavirdine 137862-53-4, Valsartan 138402-11-6, Irbesartan 139755-83-2, Sildenafil 150378-17-9, Indinavir 151687-96-6, Carbopol 974P 154598-52-4, Efavirenz 155213-67-5, Ritonavir 158966-92-8, Montelukast 159989-64-7, Nelfinavir 161279-68-1, Carbopol 971P 161814-49-9, Amprenavir 162011-90-7, Rofecoxib 169590-42-5, Celecoxib 192725-17-0, Lopinavir
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(syntactic deformable pharmaceutical foam compns.)

L15 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:185694 HCAPLUS
DOCUMENT NUMBER: 136:252483
TITLE: Clear oil-containing pharmaceutical compositions containing a therapeutic agent
INVENTOR(S): Chen, Feng-Jing; Patel, Mahesh V.; Fikstad, David T.
PATENT ASSIGNEE(S): Lipocine, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 45 pp., Cont.-in-part of U.S. Ser. No. 751,968.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 13
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20020032171	A1	20020314	US 2001-877541	20010608 <--
US 6761903	B2	20040713		
US 6267985	B1	20010731	US 1999-345615	19990630 <--
US 6309663	B1	20011030	US 1999-375636	19990817 <--
US 20010024658	A1	20010927	US 2000-751968	20001229 <--
US 6458383	B2	20021001		
US 20030077297	A1	20030424	US 2002-74687	20020211 <--
US 7374779	B2	20080520		
US 20030104048	A1	20030605	US 2002-158206	20020529 <--
US 20030235595	A1	20031225	US 2003-397969	20030325
US 20030236236	A1	20031225	US 2003-444935	20030522

PRIORITY APPLN. INFO.:

US 1999-345615	A2	19990630
US 1999-375636	A2	19990817
US 2000-751968	A2	20001229
US 1999-258654	A1	19990226
US 1999-447690	A3	19991123
WO 2000-US18807	A	20000710
US 2000-716029	A2	20001117
US 2001-800593	A2	20010306
US 2001-877541	A2	20010608
US 2001-898553	A2	20010702

ABSTRACT:

The present invention relates to pharmaceutical compns. and methods for improved solubilization of triglycerides and improved delivery of therapeutic agents. Compns. of the present invention include a carrier, where the carrier is formed from a combination of a triglyceride and at least 2 surfactants, at least one of which is hydrophilic. Upon dilution with an aqueous medium, the carrier
forms a clear, aqueous dispersion of the triglyceride and surfactants. Thus, a formulation contained soybean oil, 80, Tween-20 200, and Tween-80 800 mg.

REFERENCE COUNT: 88 THERE ARE 88 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

PI US 20020032171 A1 *20020314*

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI US 20020032171	A1	20020314	US 2001-877541	20010608	<--
US 6761903	B2	20040713			
US 6267985	B1	20010731	US 1999-345615	19990630	<--
US 6309663	B1	20011030	US 1999-375636	19990817	<--
US 20010024658	A1	20010927	US 2000-751968	20001229	<--
US 6458383	B2	20021001			
US 20030077297	A1	20030424	US 2002-74687	20020211	<--
US 7374779	B2	20080520			
US 20030104048	A1	20030605	US 2002-158206	20020529	<--
US 20030235595	A1	20031225	US 2003-397969	20030325	
US 20030236236	A1	20031225	US 2003-444935	20030522	

IT Antifoaming agents
Antioxidants
Buffers
Chelating agents
Compression
Dietary supplements
Encapsulation
Extrusion, nonbiological
Freeze drying
Granulation
Hydrophile-lipophile balance value
Lubricants
Particle size distribution
Peptidomimetics
Plasticizers
Preservatives
Surfactants
(clear oil-containing pharmaceutical compns. containing therapeutic agent)

IT *Amino acids*, biological studies
Fatty acids, biological studies
Polyoxyalkylenes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(esters; clear oil-containing pharmaceutical compns. containing therapeutic agent)

IT 50-70-4, Sorbitol, biological studies 50-70-4D, Sorbitol, esters *50-78-2*, Aspirin 56-81-5, Glycerol, biological studies 57-10-3, Palmitic acid, biological studies 57-11-4, Stearic acid, biological studies 57-55-6, Propylene glycol, biological studies 57-55-6D, 1,2-Propanediol, cyclodextrin ethers 58-32-2, Dipyridamole 58-95-7, α-Tocopherol acetate 59-02-9, α-Tocopherol 60-33-3, 9,12-Octadecadienoic acid (9Z,12Z)-, biological studies 64-17-5, Ethanol, biological studies 67-63-0, Isopropanol, biological studies 77-89-4, Acetyl triethyl citrate 77-90-7, Acetyl tributyl citrate 77-93-0, Triethyl citrate 77-94-1, Tributyl citrate 81-24-3

81-25-4 81-81-2, Warfarin 83-44-3 87-69-4D, Tartaric acid, esters 87-78-5, Mannitol 100-51-6, Benzyl alcohol, biological studies 102-76-1, Triacetin 105-37-3, Ethyl propionate 105-54-4, Ethyl butyrate 105-60-2, ε-Caprolactam, biological studies 105-60-2D, ε-Caprolactam, derivs. 106-32-1, Ethyl caprylate 107-21-1, Ethylene glycol, biological studies 107-21-1D, Ethylene glycol, esters 107-88-0, 1,3-Butanediol 110-27-0, Isopropyl myristate 111-62-6, Ethyl oleate 111-90-0, Transcutol 112-80-1, Oleic acid, biological studies 115-77-5, Pentaerythritol, biological studies 115-77-5D, Pentaerythritol, esters 115-83-3, Pentaerythritol tetrastearate 118-71-8, Maltol 119-13-1, δ-Tocopherol 122-32-7, Glyceryl trioleate 124-07-2, Octanoic acid, biological studies 127-19-5, Dimethylacetamide 128-13-2 141-22-0 142-62-1, Hexanoic acid, biological studies 142-91-6, Isopropyl palmitate 143-07-7, Lauric acid, biological studies 148-03-8, β-Tocopherol 151-41-7, Lauryl sulfate 334-48-5, Decanoic acid 360-65-6 434-13-9 463-40-1 474-25-9 475-31-0 490-23-3, β-Tocotrienol 502-44-3, ε-Caprolactone 516-35-8 516-50-7 537-40-6, Glyceryl trilinoleate 538-23-8, Glyceryl tricaprylate 538-24-9, Glyceryl trilaurate 541-15-1D, Carnitine, esters with fatty acids, salts 544-35-4, Ethyl linoleate 544-63-8, Myristic acid, biological studies 555-43-1, Glyceryl tristearate 577-11-7, Sodium docusate 616-45-5, 2-Pyrrolidone 616-45-5D, 2-Pyrrolidone, derivs. 621-70-5, Glyceryl tricaproate 621-71-6, Glyceryl tricaprate 623-84-7, Propylene glycol diacetate 640-79-9 675-20-7, 2-Piperidone 675-20-7D, 2-Piperidone, derivs. 823-22-3, δ-Caprolactone 872-50-4, N-Methylpyrrolidone, biological studies 1331-12-0, Propylene glycol monoacetate 1338-39-2, Sorbitan monolaurate 1338-41-6, Sorbitan monostearate 1338-43-8, Sorbitan monooleate 1398-61-4, Chitin 1406-18-4, Vitamin E 1721-51-3, α-Tocotrienol 1935-18-8, Palmitoylcarnitine 2466-77-5, Lauroylcarnitine 2687-91-4, N-Ethylpyrrolidone 2687-94-7, N-Octylpyrrolidone 2687-96-9, N-Lauryl-2-pyrrolidone 3068-88-0, β-Butyrolactone 3416-24-8, Glucosamine 3445-11-2 4345-03-3, α-Tocopherol succinate 5306-85-4, Dimethyl isosorbide 6493-05-6, Pentoxifylline 6990-06-3, Fusidic acid 7616-22-0, γ-Tocopherol 7664-93-9D, Sulfuric acid, alkyl esters, salts 8007-43-0, Sorbitan sesquioleate 9002-89-5, Polyvinylalcohol 9002-92-0, Polyethylene glycol lauryl ether 9002-96-4 9003-39-8, Polyvinylpyrrolidone 9003-39-8D, PVP, conjugates with phosphatidylethanolamines 9004-34-6D, Cellulose, derivs. 9004-54-0, Dextran, biological studies 9004-57-3, Ethyl cellulose 9004-61-9, Hyaluronic acid 9004-65-3, Hydroxypropyl methyl cellulose 9004-67-5, Methyl cellulose 9004-74-4, Methoxy polyethylene glycol 9004-81-3, Polyethylene glycol monolaurate 9004-95-9, Polyethylene glycol cetyl ether 9004-96-0, Polyethylene glycol oleate 9004-98-2, Polyethylene glycol oleyl ether 9004-99-3, Polyethylene glycol monostearate 9005-00-9, Polyethylene glycol stearyl ether 9005-02-1, Polyethylene glycol dilaurate 9005-07-6, Polyethylene glycol dioleate 9005-08-7, Polyethylene glycol distearate 9005-25-8, Starch, biological studies 9005-32-7D, Alginic acid, salts 9005-37-2, Propylene glycol alginate 9005-49-6, Heparin, biological studies 9005-64-5, Polysorbate 20 9005-65-6, Polysorbate 80 9005-66-7, Tween 40 9005-67-8, Tween 60 9007-27-6, Chondroitin 9007-48-1, Polyglyceryl oleate 9009-32-9, Polyglyceryl stearate 9014-63-5, Xylan 9016-45-9, Polyethylene glycol nonyl phenyl ether 9041-08-1, Heparin sodium 9050-30-0, Heparan sulfate 9050-36-6, Maltodextrin 9062-73-1, Polyethylene glycol sorbitan laurate 9062-90-2, Polyethylene glycol sorbitan oleate 10041-19-7 11140-04-8, Imwitor 988 12619-70-4, Cyclodextrin 12619-70-4D, Cyclodextrin, hydroxypropyl ethers 12772-47-3, Pentaerythritol oleate 13027-26-4, δ-Tocopherol

acetate 13081-97-5, Pentaerythritol distearate 13552-80-2, Glyceryl triundecanoate 14101-61-2, γ-Tocotrienol 14440-80-3, Stearoyl-2 Lactylate 14465-68-0, Glyceryl trilinolenate 14605-22-2 22373-05-3, β-Tocopherol acetate 22373-06-4, γ-Tocopherol acetate 22882-95-7, Isopropyl linoleate 25168-73-4, Sucrose monostearate 25249-06-3, Polygalacturonic acid 25322-68-3D, ethers or esters 25322-69-4D, Polypropylene glycol, esters 25339-99-5, Sucrose monolaurate 25612-59-3, δ-Tocotrienol 25618-55-7D, Polyglycerol, esters with fatty acids 25637-97-2, Sucrose dipalmitate 26266-57-9, Sorbitan monopalmitate 26266-58-0, Sorbitan trioleate 26446-38-8, Sucrose monopalmitate 26658-19-5, Sorbitan tristearate 27195-16-0, Sucrose distearate 27321-96-6, Polyethylene glycol cholesteryl ether 29874-09-7, Myristoylcarnitine 29894-36-8, Polymannuronic acid 31692-85-0, Glycofurol 31694-55-0D, AMD triesters with fatty acids 35296-72-1, Butanol 36291-32-4, Citric acid monoglyceride 37270-89-6, Nadroparin calcium 51938-44-4, Sorbitan sesquistearate 53168-42-6, Myvacet 9-45 54392-26-6, Sorbitan monoisostearate 55142-85-3, Ticlid 56451-84-4 57307-93-4, Pentaerythritol caprylate 61725-93-7, Polyglyceryl distearate 61752-68-9, Sorbitan tetrastearate 64480-66-6, Glycoursodeoxycholic acid 68818-37-1, Pentaerythritol decanoate 68958-64-5, Polyethylene glycol glyceryl trioleate 69070-98-0 70226-44-7, Heparan 73963-72-1, Cilostazol 74504-64-6, Polyglyceryl laurate 75634-40-1, Dermatan 83138-62-9, Polyglyceryl isostearate 88662-03-7 93790-70-6, Cholylsarcosine 93790-72-8, N-Methyltaurocholic acid 98913-68-9, Pentaerythritol isostearate 106392-12-5, Polyethylene glycol-polypropylene glycol block copolymer 110540-43-7, Polyglyceryl pentaoleate 113665-84-2, Clopidogrel 128254-89-7 128254-90-0 128286-20-4 146478-45-7, Polyglyceryl dioleate 148796-42-3 150372-93-3, Polyoxyethylene glyceryl laurate 162011-90-7, Rofecoxib 181695-72-7, Valdecoxib 198470-84-7, Parecoxib 208666-87-9, Captex 810D 256923-73-6, γ-Tocotrienol acetate 300583-65-7 300583-68-0 403815-06-5 403815-07-6 403815-12-3 403821-12-5, Polyglyceryl trioleate 403838-29-9
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(clear oil-containing pharmaceutical compns. containing therapeutic agent)

L15 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:71842 HCAPLUS
DOCUMENT NUMBER: 136:123661
TITLE: Stable salts of o-acetylsalicylic acid with basic *amino acids*
INVENTOR(S): Franckowiak, Gerhard; Appolt, Hubert; Leifker, Gregor; Wirges, Hans-Peter; Ledwoch, Wolfram
PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002005782	A2	20020124	WO 2001-EP7669	20010705 <--
WO 2002005782	A3	20031002		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,

RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

DE 10034802	A1	20020131	DE 2000-10034802	20000718	<--
CA 2416288	A1	20030115	CA 2001-2416288	20010705	<--
BR 2001012538	A	20030909	BR 2001-12538	20010705	<--
HU 2003002053	A2	20030929	HU 2003-2053	20010705	<--
EP 1365737	A2	20031203	EP 2001-956511	20010705	<--
EP 1365737	B1	20050420			

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2004507463	T	20040311	JP 2002-511715	20010705	<--
AU 2001278471	B2	20040722	AU 2001-278471	20010705	<--
AT 293589	T	20050515	AT 2001-956511	20010705	<--
ES 2241849	T3	20051101	ES 2001-956511	20010705	<--
SK 286162	B6	20080407	SK 2003-67	20010705	<--
US 20020091108	A1	20020711	US 2001-906497	20010716	<--
US 6773724	B2	20040810			
IN 2003MN00014	A	20051021	IN 2003-MN14	20030102	
NO 2003000222	A	20030116	NO 2003-222	20030116	
MX 2003PA00510	A	20040420	MX 2003-PA510	20030117	
ZA 2003000469	A	20040621	ZA 2003-469	20030117	
KR 773658	B1	20071105	KR 2003-700713	20030117	
HR 2003000108	B1	20061231	HR 2003-108	20030217	
HK 1061811	A1	20060127	HK 2004-104934	20040707	
US 20050009791	A1	20050113	US 2004-915652	20040809	
AU 2004218728	A1	20041028	AU 2004-218728	20041013	
AU 2004218728	B2	20061109			

PRIORITY APPLN. INFO.:	DE 2000-10034802	A	20000718
	AU 2001-278471	A3	20010705
	WO 2001-EP7669	W	20010705
	US 2001-906497	A3	20010716

ABSTRACT:
The invention relates to stable salts of o-acetylsalicylic acid with basic ***amino*** *acids*, to a method for producing them and to their use as drugs. Thus 9.9 kg acetylsalicylic acid were dissolved in 120 kg ethanol at 20-25°C; a solution of 9.0 kg *lysine* hydrate and 26.5 kg water were added while 30°C was not exceeded; crystallization was initiated with 50 g inoculation crystals, acetone, and cooling to 0°C. Crystals were filtered, centrifuged and dried below 40°C and 30 mbar. The yield was 89-94% ; residual moisture 0.10-0.15%.

TI Stable salts of o-acetylsalicylic acid with basic *amino acids*

PI WO 2002005782 A2 *20020124*

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI WO 2002005782	A2	20020124	WO 2001-EP7669	20010705	<--
WO 2002005782	A3	20031002			

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG,

KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

DE 10034802	A1	20020131	DE 2000-10034802	20000718 <--
CA 2416288	A1	20030115	CA 2001-2416288	20010705 <--
BR 2001012538	A	20030909	BR 2001-12538	20010705 <--
HU 2003002053	A2	20030929	HU 2003-2053	20010705 <--
EP 1365737	A2	20031203	EP 2001-956511	20010705 <--
EP 1365737	B1	20050420		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2004507463	T	20040311	JP 2002-511715	20010705 <--
AU 2001278471	B2	20040722	AU 2001-278471	20010705 <--
AT 293589	T	20050515	AT 2001-956511	20010705 <--
ES 2241849	T3	20051101	ES 2001-956511	20010705 <--
SK 286162	B6	20080407	SK 2003-67	20010705 <--
US 20020091108	A1	20020711	US 2001-906497	20010716 <--
US 6773724	B2	20040810		
IN 2003MN00014	A	20051021	IN 2003-MN14	20030102
NO 2003000222	A	20030116	NO 2003-222	20030116
MX 2003PA00510	A	20040420	MX 2003-PA510	20030117
ZA 2003000469	A	20040621	ZA 2003-469	20030117
KR 773658	B1	20071105	KR 2003-700713	20030117
HR 2003000108	B1	20061231	HR 2003-108	20030217
HK 1061811	A1	20060127	HK 2004-104934	20040707
US 20050009791	A1	20050113	US 2004-915652	20040809
AU 2004218728	A1	20041028	AU 2004-218728	20041013
AU 2004218728	B2	20061109		

AB The invention relates to stable salts of o-acetylsalicylic acid with basic *amino acids*, to a method for producing them and to their use as drugs. Thus 9.9 kg acetylsalicylic acid were dissolved in 120 kg ethanol at 20-25°C; a solution of 9.0 kg *lysine* hydrate and 26.5 kg water were added while 30°C was not exceeded; crystallization was initiated with 50 g inoculation crystals,. . .

ST stable salt o acetylsalicylic basic *amino acid*; *lysine* acetylsalicylate stable salt basic *amino acid*

IT Purinoceptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(P2T, inhibitors; stable salts of o-acetylsalicylic acid with basic *amino acids*)

IT *Amino acids*, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(basic; stable salts of o-acetylsalicylic acid with basic *amino acids*)

IT Crystallization
(cocrystn.; stable salts of o-acetylsalicylic acid with basic *amino acids*)

IT Heart, disease
(infarction, therapeutic agents; stable salts of o-acetylsalicylic acid with basic *amino acids*)

IT Thrombin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; stable salts of o-acetylsalicylic acid with basic *amino acids*)

IT Muscle, disease
Pain
(myalgia, treatment of; stable salts of o-acetylsalicylic acid with basic *amino acids*)

IT Antiarthritics
Antimigraine agents
Calcium channel blockers
Crystallization
Nervous system agents
Particle size distribution
Stability
(stable salts of o-acetylsalicylic acid with basic *amino acids*)

IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(αIIbβ3, inhibitors; stable salts of o-acetylsalicylic acid with basic *amino acids*)

IT 62952-06-1P, *Lysine* acetylsalicylate
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cocrystn. with glycine; stable salts of o-acetylsalicylic acid with basic *amino acids*)

IT 56-40-6, Glycine, biological studies
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(cocrystn. with *lysine* acetylsalicylate; stable salts of o-acetylsalicylic acid with basic *amino acids*)

IT 9002-05-5, Blood coagulation factor Xa
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; stable salts of o-acetylsalicylic acid with basic *amino acids*)

IT 67-64-1, Acetone, processes
RL: PEP (Physical, engineering or chemical process); PROC (Process)
(stable salts of o-acetylsalicylic acid with basic *amino acids*)

IT *50-78-2*, o-Acetylsalicylic acid 56-87-1, L-*Lysine*, reactions 70-54-2, *Lysine*
RL: RCT (Reactant); RACT (Reactant or reagent)
(stable salts of o-acetylsalicylic acid with basic *amino acids*)

IT *50-78-2DP*, o-Acetylsalicylic acid, basic *amino acid* salts of 37933-78-1P, *Lysine* acetylsalicylate
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(stable salts of o-acetylsalicylic acid with basic *amino acids*)

IT 70-26-8D, L-Ornithine, salt with o-acetylsalicylic acid 71-00-1D, L-Histidine, salt with o-acetylsalicylic acid 74-79-3D, L-*Arginine*, salt with o-acetylsalicylic acid 305-62-4D, salt with o-acetylsalicylic acid
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stable salts of o-acetylsalicylic acid with basic *amino acids*)

L15 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:279689 HCAPLUS
DOCUMENT NUMBER: 130:316634
TITLE: Intraarticular preparation for treatment of arthropathy
INVENTOR(S): Suzuki, Makoto; Ishigaki, Kenji; Okada, Minoru; Ono, Kenji; Kasai, Shuichi; Imamori, Katsumi
PATENT ASSIGNEE(S): SSP Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 28 pp.

CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 911025	A1	19990428	EP 1998-119414	19981014 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TW 577758	B	20040301	TW 1998-87116891	19981012 <--
US 6197326	B1	20010306	US 1998-172271	19981014 <--
JP 11222425	A	19990817	JP 1998-293385	19981015 <--
CA 2251277	A1	19990427	CA 1998-2251277	19981020 <--
CN 1215589	A	19990505	CN 1998-124109	19981027 <--
US 6428804	B1	20020806	US 2000-706762	20001107 <--

PRIORITY APPLN. INFO.: JP 1997-294009 A 19971027
US 1998-172271 A1 19981014

ABSTRACT:
This invention relates to an intra-articular preparation for the treatment of arthropathy, which comprises microcapsules of (a) a high-mol. substance, which has biodegradability and biocompatibility, and (b) a drug. When applied directly to a joint area, this preparation can achieve a high drug concentration at the
target area, can inhibit occurrence of general side effect, and can maintain drug efficacy over a long term. The preparation can therefore alleviate the burden on the patient. Microcapsules were prepared from lactic acid-glycolic acid copolymer 4.5, beclomethasone propionate 0.5 g and other ingredients, and their ***particle*** *sizes* and pharmacokinetic parameters were tested.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

PI EP 911025 A1 *19990428*

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 911025	A1	19990428	EP 1998-119414	19981014 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TW 577758	B	20040301	TW 1998-87116891	19981012 <--
US 6197326	B1	20010306	US 1998-172271	19981014 <--
JP 11222425	A	19990817	JP 1998-293385	19981015 <--
CA 2251277	A1	19990427	CA 1998-2251277	19981020 <--
CN 1215589	A	19990505	CN 1998-124109	19981027 <--
US 6428804	B1	20020806	US 2000-706762	20001107 <--

AB . . . the patient. Microcapsules were prepared from lactic acid-glycolic acid copolymer 4.5, beclomethasone propionate 0.5 g and other ingredients, and their *particle sizes* and pharmacokinetic parameters were tested.

IT *Amino acids*, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polymers; intraarticular prepns. for treatment of arthropathy containing microcapsules of high-mol. substances and pharmaceutically active agents)

IT 50-02-2, Dexamethasone 50-18-0, Cyclophosphamide 50-21-5D, Lactic acid, polymers 50-23-7, Hydrocortisone 50-24-8, Prednisolone *50-78-2*, Aspirin 52-67-5, D-Penicillamine 53-86-1, Indomethacin 59-05-2, Methotrexate 69-72-7, Salicylic acid, biological studies 79-14-1D, Glycolic acid, polymers 83-43-2, Methylprednisolone

96-48-0D, Butyrolactone, polymers 108-29-2D, polymers 124-94-7, Triamcinolone 378-44-9, Betamethasone 446-86-6, Azathioprine 502-44-3D, Caprolactone, polymers 530-78-9, Flufenamic acid 599-79-1, Salazosulfapyridine 1177-87-3, Dexamethasone acetate 1320-61-2D, Hydroxybutyrate, polymers 2392-39-4, Dexamethasone sodium phosphate 4419-39-0, Beclomethasone 5104-49-4, Flurbiprofen 5534-09-8, Beclomethasone dipropionate 9004-61-9, Hyaluronic acid 9005-25-8, Starch, biological studies 9007-28-7, Chondroitin sulfate 9012-76-4, Chitosan 9067-32-7, Sodium hyaluronate 12244-57-4, Gold sodium thiomalate 13710-19-5, Tolfenamic acid 13799-03-6, Protizinic acid 15307-79-6, Diclofenac sodium 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 15802-18-3D, alkyl derivs. polymers 20423-99-8, Deprodone 21256-18-8, Oxaprozin 22071-15-4, Ketoprofen 22494-42-4, Diflunisal 23779-99-9, Floctafenine 33005-95-7, Tiaprofen 34031-32-8, Auranofin 34346-01-5, Lactic acid-glycolic acid copolymer 36322-90-4, Piroxicam 36330-85-5, Fenbufen 38194-50-2, Sulindac 39718-89-3, Alminoprofen 42924-53-8, Nabumetone 50924-49-7, Mizoribine 53164-05-9, Acemetacin 57132-53-3, Proglumetacin 57781-15-4, Halopredone 59804-37-4, Tenoxicam 63329-53-3, Lobenzarit 65002-17-7, Bucillamine 68767-14-6, Loxoprofen 71125-38-7, Meloxicam 74711-43-6, Zaltoprofen 79217-60-0, Cyclosporin 91503-79-6, Flurbiprofen axetil 99464-64-9, Ampiroxicam
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(intraarticular prepns. for treatment of arthropathy containing microcapsules of high-mol. substances and pharmaceutically active agents)

L15 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:769812 HCAPLUS
DOCUMENT NUMBER: 128:53123
ORIGINAL REFERENCE NO.: 128:10313a
TITLE: Polarizing microscopy of crystalline drugs based on the crystal habit determination for the purpose of a rapid estimation of crystal habits, *particle sizes* and specific surface areas of small crystals
AUTHOR(S): Watanabe, Atsushi
CORPORATE SOURCE: Kenbikogaku-kenkyusho, Ltd., Ashiya, 659, Japan
SOURCE: Yakugaku Zasshi (*1997*), 117(10-11), 771-785
CODEN: YKKZAJ; ISSN: 0031-6903
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
ABSTRACT:
In 1939,the author reported the results of measured refractive indexes of about a hundred crystalline drugs listed in [Japanese Pharmacopeia (JP V)] at the Takeda Research Laboratory using a Leitz PM polarizing microscope and newly developed immersion oils. When the author had reopened the study of crystalline drugs using a polarizing microscope at the Kobe-Gakuin University starting from 1975 one of the main purposes was to clarify the relation between crystal habits and refractive indexes. In most cases of crystal habits, refractive indexes were uniquely measured from a predominant pair of faces forming superior the habit, and they were called as "key refractive indexes". The author and his co-workers tried to investigate the possibility of measuring the key refractive indexes widely from all the obtainable crystalline drugs listed in the [JP X] or [JP XI], co-operating with the Pharmacy of Kobe University Hospital. Thus, more than 170 kinds of crystalline drugs were tested for their key refractive indexes and found that they were measured from about 60-70% of tested drugs. It was also clarified that the difference of 2 key refractive indexes, (n2-n1), the birefringence of the section, was also an unique invariable number for the habit,

and it played an important role not only for the graphic representation of log(n2-n1), abscissa, against (n1, n2), ordinate, for the sake of an anal. purpose but also to measure a thickness of a section (habit) using a retardation color. The similarity of crystal habits in the microscopic field was based on the facts of measuring the same key refractive indexes, and the author had developed a chart for measuring key refractive indexes as well as producing a 3-dimensional orthog. projection of a crystal habit simultaneously applying a thickness measuring method using a birefringence. Using the similarity in crystal habits, the distributions of *particle* ***sizes*** and sp. surface areas of all the crystals in the microscopic field had been calculated by a personal computer putting in necessary habit coeffs. The relation between 2 dispersions of *particle sizes* in log (V) and sp. surface areas in log (SSA) were shown under the rectangular coordinates log (V) on the abscissa and log (SSA) on the ordinate, where the loci of log (SSA) formed simple striped pattern composed of parallel straight lines depending on habit coeffs. It would be possible to estimate the value of a sp. surface area of any crystalline substance by plotting the value of log (V) on the straight line of a locus of log (SSA) having the same habit coeffs.

TI . . . microscopy of crystalline drugs based on the crystal habit determination for the purpose of a rapid estimation of crystal habits, *particle sizes* and specific surface areas of small crystals

SO Yakugaku Zasshi (*1997*), 117(10-11), 771-785
CODEN: YKKZAJ; ISSN: 0031-6903

AB . . . crystal habit simultaneously applying a thickness measuring method using a birefringence. Using the similarity in crystal habits, the distributions of *particle sizes* and sp. surface areas of all the crystals in the microscopic field had been calculated by a personal computer putting in necessary habit coeffs. The relation between 2 dispersions of *particle sizes* in log (V) and sp. surface areas in log (SSA) were shown under the rectangular coordinates log (V) on the. . .

ST polarization microscopy crystal drug; crystal habit drug polarization microscopy; surface area drug polarization microscopy; *particle size* drug polarization microscopy

IT Birefringence
Crystal morphology
Drugs
Particle size distribution
Surface area
(polarizing microscopy of crystalline drugs based on crystal habit determination)

IT 50-02-2, Dexamethasone 50-06-6, Phenobarbital, biological studies 50-14-6, Ergocalciferol 50-18-0, Cyclophosphamide 50-33-9, Phenylbutazone, biological studies 50-34-0, Propantheline bromide 50-44-2, Mercaptopurine 50-49-7, Imipramine 50-53-3, Chlorpromazine, biological studies 50-54-4, Quinidine sulfate 50-59-9, Cephaloridine *50-78-2*, Aspirin 50-81-7, Ascorbic acid, biological studies 50-99-7, Glucose, biological studies 51-06-9, Procainamide 51-43-4, Epinephrine 52-86-8, Haloperidol 53-86-1, Indomethacin 54-21-7, Sodium salicylate 54-85-3, Isoniazid 55-98-1, Busulfan 56-75-7, Chloramphenicol 56-87-1, L-*Lysine*, biological studies 57-41-0, Phenytoin 57-43-2, Amobarbital 57-44-3, Barbital 57-66-9, Probenecid 57-94-3, Tubocurarine chloride 58-25-3, Chlordiazepoxide 58-39-9, Perphenazine 58-71-9, Cephalothin sodium 58-73-1, Diphenhydramine 58-93-5, Hydrochlorothiazide 59-30-3, Folic acid, biological studies 59-46-1, Procaine 59-66-5, Acetazolamide 59-67-6, Nicotinic acid, biological studies 59-92-7, Levodopa, biological studies

60-54-8, Tetracycline 60-56-0, Thiamazole 62-44-2, Phenacetin 63-42-3, Lactose 63-68-3, L-Methionine, biological studies 63-91-2, L-Phenylalanine, biological studies 64-77-7, Tolbutamide 65-85-0, Benzoic acid, biological studies 67-03-8, Thiamine hydrochloride 67-73-2, Fluocinolone acetonide 68-19-9, Cyanocobalamin 68-41-7, Cycloserine 68-89-3, Sulpyrine 69-43-2, Prenylamine lactate 69-53-4, Ampicillin 69-72-7, Salicylic acid, biological studies 71-27-2, Suxamethonium chloride 71-63-6, Digitoxin 72-18-4, L-Valine, biological studies 72-19-5, L-Threonine, biological studies 73-22-3, L-Tryptophan, biological studies 73-32-5, L-Isoleucine, biological studies 74-55-5, Ethambutol 76-25-5, Triamcinolone acetonide 77-09-8, Phenolphthalein 77-65-6, Bromdiethylacetylurea 77-92-9, Citric acid, biological studies 80-77-3, Chlormezanone 83-75-0, Quinine ethylcarbonate 83-88-5, Riboflavin, biological studies 84-02-6, Prochlorperazine maleate 94-20-2, Chlorpropamide 95-25-0, Chlorzoxazone 98-92-0, Nicotinamide 98-96-4, Pyrazinamide 113-92-8, Chlorpheniramine maleate 113-98-4, Benzylpenicillin potassium 114-07-8, Erythromycin 119-48-2, Dimorpholamine 121-54-0, Benzethonium chloride 125-33-7, Primidone 125-69-9, Dextromethorphan hydrobromide 126-07-8, Griseofulvin 127-48-0, Trimethadione 127-69-5, Sulfisoxazole 129-03-3, Cyproheptadine 129-20-4, Oxyphenbutazone 130-95-0, Quinine 132-92-3, Methicillin sodium 132-93-4, Phenethicillin potassium 132-98-9, Phenoxymethylpenicillin potassium 133-15-3, Calcium p-aminosalicylate 133-67-5, Trichlormethiazide 137-08-6, Calcium pantothenate 137-58-6, Lidocaine 144-11-6, Trihexyphenidyl 144-55-8, Sodium bicarbonate, biological studies 298-46-4, Carbamazepine 299-42-3, Ephedrine 304-20-1, Hydralazine hydrochloride 315-30-0, Allopurinol 343-55-5, Dicloxacillin Sodium 378-44-9, Betamethasone 396-01-0, Triamterene 439-14-5, Diazepam 464-49-3 481-06-1, Santonin 496-67-3, Bromovalerylurea 515-64-0, Sulfisomidine 523-87-5, Dimenhydrinate 525-66-6, Propranolol 530-43-8, Chloramphenicol palmitate 532-32-1, Sodium benzoate 532-43-4, Thiamine nitrate 564-25-0, Doxycycline 590-63-6 751-97-3, Rolitetracycline 814-80-2, Calcium lactate 912-60-7, Noscapine hydrochloride 968-81-0, Acetohexamide 1264-62-6, Erythromycin ethyl succinate 1400-61-9, Nystatin 1642-54-2, Diethylcarbamazine citrate 2152-44-5, Betamethasone valerate 2276-90-6 3166-62-9, Methylbenactyzium bromide 3485-14-1, Ciclacillin 7104-38-3, Levomepromazine maleate 7177-48-2, Ampicillin trihydrate 7447-40-7, Potassium chloride, biological studies 7647-14-5, Sodium chloride, biological studies 7681-11-0, Potassium iodide, biological studies 7733-02-0, Zinc sulfate 7758-02-3, Potassium bromide, biological studies 7772-98-7, Sodium thiosulfate 13840-56-7, Sodium borate 14222-60-7, Prothionamide 15686-71-2, Cephalexin 15826-37-6, Sodium cromoglycate 16846-24-5, Josamycin 17575-22-3, Lanatoside C 22465-48-1 27164-46-1, Cefazolin sodium 29825-08-9 37721-39-4, Phenovalin
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polarizing microscopy of crystalline drugs based on crystal habit determination)

L15 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1971:480281 HCAPLUS
DOCUMENT NUMBER: 75:80281
ORIGINAL REFERENCE NO.: 75:12701a,12704a
TITLE: Free-flowing, easily wettable particles containing acetylsalicylic acid
INVENTOR(S): Boncey, Graham A.; Hedge, Marice J.; Henderson, James Rae

PATENT ASSIGNEE(S): Aspro-Nicholas Ltd.
SOURCE: Ger. Offen., 25 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2058434	A	19710603	DE 1970-2058434	19701127 <--
DE 2058434	B2	19800424		
DE 2058434	C3	19801218		
GB 1287475	A	19720831	GB 1969-58203	19691128 <--
ZA 7007915	A	19710825	ZA 1970-7915	19701123 <--
US 3882228	A	19750506	US 1970-92284	19701123 <--
IL 35714	A	19740314	IL 1970-35714	19701124 <--
IN 129401	A1	19750816	IN 1970-129401	19701126 <--
NL 7017417	A	19710602	NL 1970-17417	19701127 <--
NL 165928	B	19810115		
NL 165928	C	19810615		
FR 2073431	A5	19711001	FR 1970-42668	19701127 <--
FR 2073431	B1	19740322		
AT 302533	B	19721025	AT 1970-10713	19701127 <--
ES 385974	A1	19730501	ES 1970-385974	19701127 <--
CA 948108	A1	19740528	CA 1970-99296	19701127 <--
DK 130453	B	19750224	DK 1970-6054	19701127 <--
SE 383099	B	19760301	SE 1970-16129	19701127 <--
JP 51006727	B	19760302	JP 1970-105390	19701128 <--
US 3887700	A	19750603	US 1973-415247	19731112 <--

PRIORITY APPLN. INFO.: GB 1969-58203 A 19691128
US 1970-92284 A3 19701123

ABSTRACT:
The title preparation consists of acetylsalicylic acid particles coated with one or more of the following compds. m. >105°. low mol. weight *amino* ***acids*** (glycine, methionine), sugars (sucrose, lactose, sugar polymers), sugar alcs. (mannitol, inositol, sorbitol) or mixts. thereof. In addition, the coat contains a wetting agent (cationic, anionic, nonionic types) and (or) a film-forming agent [gums, cellulose derivs., poly(vinylpyrrolidone)]. The ratio of acetylsalicylic acid to the total coating material is preferably between 7.1 to 1.1. Thus, the acetylsalicylic acid is suspended in an aqueous solution of the wetting agent. The suspension is treated with a small portion of an aqueous solution of the coating material and film-forming agent to form a thin paste. After the remaining solution of coating material and film-forming agent is added, the suspension obtained is stirred continuously and spray-dried to small ***particles*** of which 95% should have a *particle size* <105 μ. Thus coated acetylsalicylic acid particles may be made into water soluble powder or tablets or into effervescent powder or tablets. Six examples are given.

PI DE 2058434 *19710603*

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 2058434	A	19710603	DE 1970-2058434	19701127 <--
DE 2058434	B2	19800424		
DE 2058434	C3	19801218		
GB 1287475	A	19720831	GB 1969-58203	19691128 <--
ZA 7007915	A	19710825	ZA 1970-7915	19701123 <--
US 3882228	A	19750506	US 1970-92284	19701123 <--

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     IL 35714           A     19740314    IL 1970-35714          19701124 <--
     IN 129401          A1    19750816    IN 1970-129401         19701126 <--
     NL 7017417         A     19710602    NL 1970-17417          19701127 <--
     NL 165928          B     19810115
     NL 165928          C     19810615
     FR 2073431         A5    19711001    FR 1970-42668          19701127 <--
     FR 2073431         B1    19740322
     AT 302533          B     19721025    AT 1970-10713          19701127 <--
     ES 385974          A1    19730501    ES 1970-385974         19701127 <--
     CA 948108          A1    19740528    CA 1970-99296          19701127 <--
     DK 130453          B     19750224    DK 1970-6054           19701127 <--
     SE 383099          B     19760301    SE 1970-16129          19701127 <--
     JP 51006727        B     19760302    JP 1970-105390         19701128 <--
     US 3887700         A     19750603    US 1973-415247         19731112 <--
AB   . . . preparation consists of acetylsalicylic acid particles coated with one
     or more of the following compds. m. >105°. low mol. weight
     amino acids (glycine, methionine), sugars (sucrose,
     lactose, sugar polymers), sugar alcs. (mannitol, inositol, sorbitol) or
     mixts. thereof. In addition, the coat contains. . . remaining solution of
     coating material and film-forming agent is added, the suspension obtained
     is stirred continuously and spray-dried to small particles of
     which 95% should have a particle size <105 μ. Thus
     coated acetylsalicylic acid particles may be made into water soluble powder
     or tablets or into effervescent powder. . .
IT   50-78-2, biological studies
     RL: BIOL (Biological study)
        (pharmaceutical powders, coated)


=>
=> s (Franckowiak G? or Appolt H? or Leifker G? or Wirges H? or Ledwoch W?)/au
L16        158 (FRANCKOWIAK G? OR APPOLT H? OR LEIFKER G? OR WIRGES H? OR LEDWO
               CH W?)/AU

=>

=> d his

     (FILE 'HOME' ENTERED AT 03:57:55 ON 13 JUL 2008)

     FILE 'CAPLUS' ENTERED AT 03:58:20 ON 13 JUL 2008
L1             0 S 2000DE-10034802.5/PN
L2             1 S DE-10034802.5/PN

     FILE 'REGISTRY' ENTERED AT 04:31:04 ON 13 JUL 2008
                E O-ACETYLSALICYLIC ACID/CN
L3             5 S E3-E7

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 04:32:36 ON 13 JUL 2008
L4        184079 S L3
L5          1385 S    (ACETYLSALICYCLIC OR 0-ACETYLSALICYCLIC) (W) ACID?
L6        184547 S L5 OR L4
L7       3449848 S LYSINE OR ARGININE OR AMINOBUTYRIC OR OMITHINE OR AMINO (W) A
L8          4660 S L6 AND L7
L9       2087871 S PARTICLE (S) SIZE OR DIAMETER OR RADIUS
L10           83 S L8 AND L9
L11           66 DUP REM L10 (17 DUPLICATES REMOVED)
L12         1385 S  (ACETYLSALICYCLIC OR 0-ACETYLSALICYCLIC) (W) ACID?
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L13           0 S L12 AND L11
L14          34 S L11 AND (AY<=2002 OR PY<=2002)
L15          10 S PARTICLE (S) (SIZE OR DIAMETER OR RADIUS) AND L14
L16         158 S (FRANCKOWIAK G? OR APPOLT H? OR LEIFKER G? OR WIRGES H? OR LE

=> s l11 and l16
L17          3 L11 AND L16

=> d ibib iabs kwic 1-3

L17  ANSWER 1 OF 3  HCAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2006:1283517  HCAPLUS
DOCUMENT NUMBER:          146:50295
TITLE:                    Stabile active ingredient complex of salts of the
                          O-acetylsalicylic acid with basic amino
                          acids and glycine
INVENTOR(S):              Franckowiak, Gerhard; Ledwoch,
                          Wolfram; Schweinheim, Eberhard; Hayauchi, Yutaka
PATENT ASSIGNEE(S):       Bayer Healthcare A.-G., Germany
SOURCE:                   PCT Int. Appl., 14pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 German
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 2006128600         A2    20061207    WO 2006-EP4799          20060520
     WO 2006128600         A3    20070426
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
             KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
             MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
             SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
             VN, YU, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA
     DE 102005025283       A1    20061207    DE 2005-102005025283    20050602
     AU 2006254429         A1    20061207    AU 2006-254429          20060520
     CA 2610194            A1    20061207    CA 2006-2610194         20060520
     EP 1890994            A2    20080227    EP 2006-743005          20060520
         R:  AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL,
             BA, HR, MK, YU
     IN 2007DN09158        A     20080118    IN 2007-DN9158          20071128
     MX 200714988          A     20080215    MX 2007-14988           20071128
     NO 2007006592         A     20071220    NO 2007-6592            20071220
     KR 2008030578         A     20080404    KR 2007-730689          20071228
PRIORITY APPLN. INFO.:                       DE 2005-102005025283A   20050602
                                             WO 2006-EP4799      W   20060520

ABSTRACT:
The invention relates to stabile active ingredient complexes of salts of the
o-acetylsalicylic acid with basic amino acids and glycine,
to a method for producing the same and to their use as drugs.  Thus 40.0 kg
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O-acetylsalicylic acid in 500 kg ethanol was mixed with 36.4 kg DL-***lysine*** monohydrate in 110 kg water. 20 G inoculation crystals were added followed by mixing in 490 kg acetone and a suspension containing 8,0 kg glycine in 25 kg water and 90 kg ethanol. The crystal mixture was isolated and dried; 60-70 kg DL-*lysine* acetylsalicylate with 10% glycine was obtained with medium *particle size* of 41 μm. The whole procedure was carried out under sterile conditions.

TI Stabile active ingredient complex of salts of the O-acetylsalicylic acid with basic *amino acids* and glycine

IN *Franckowiak, Gerhard*; *Ledwoch, Wolfram*; Schweinheim, Eberhard; Hayauchi, Yutaka

AB The invention relates to stabile active ingredient complexes of salts of the o-acetylsalicylic acid with basic *amino acids* and glycine, to a method for producing the same and to their use as drugs. Thus 40.0 kg O-acetylsalicylic acid in 500 kg ethanol was mixed with 36.4 kg DL-*lysine* monohydrate in 110 kg water. 20 G inoculation crystals were added followed by mixing in 490 kg acetone and a. . . 8,0 kg glycine in 25 kg water and 90 kg ethanol. The crystal mixture was isolated and dried; 60-70 kg DL-*lysine* acetylsalicylate with 10% glycine was obtained with medium *particle size* of 41 μm. The whole procedure was carried out under sterile conditions.

ST *lysine* acetylsalicylate glycine crystn

IT *Amino acids*, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(basic; stabile active ingredient complex of salts of O-acetylsalicylic acid with basic *amino acids* and glycine)

IT Pharmaceutical injections
(i.a. injections; stabile active ingredient complex of salts of O-acetylsalicylic acid with basic *amino acids* and glycine)

IT Pharmaceutical injections
(i.m. injections; stabile active ingredient complex of salts of O-acetylsalicylic acid with basic *amino acids* and glycine)

IT Pharmaceutical injections
(i.p. injections; stabile active ingredient complex of salts of O-acetylsalicylic acid with basic *amino acids* and glycine)

IT Pharmaceutical injections
(i.v. injections; stabile active ingredient complex of salts of O-acetylsalicylic acid with basic *amino acids* and glycine)

IT Pharmaceutical injections
(intracardial, intraspinal, intralumbar, intracutaneous; stabile active ingredient complex of salts of O-acetylsalicylic acid with basic *amino acids* and glycine)

IT Headache
(migraine; stabile active ingredient complex of salts of O-acetylsalicylic acid with basic *amino acids* and glycine)

IT Muscle, disease
Pain
(myalgia; stabile active ingredient complex of salts of O-acetylsalicylic acid with basic *amino acids* and glycine)

IT Nerve, disease
Pain
(neuralgia; stabile active ingredient complex of salts of

O-acetylsalicylic acid with basic amino acids and glycine)

IT Pharmaceutical injections
(s.c. injections; stabile active ingredient complex of salts of O-acetylsalicylic acid with basic amino acids and glycine)

IT Angina pectoris
Angioplasty
Arthritis
Coronary angioplasty
Coronary bypass surgery
Crystallization
Freeze drying
Infusion drug delivery systems
Ischemia
Melting point
Myocardial infarction
Parenteral drug delivery systems
Particle size
Stability
Stroke
(stabile active ingredient complex of salts of O-acetylsalicylic acid with basic amino acids and glycine)

IT Medical goods
(stents, implantation; stabile active ingredient complex of salts of O-acetylsalicylic acid with basic amino acids and glycine)

IT 50-78-2, O-Acetylsalicylic acid 885701-25-7
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(stabile active ingredient complex of salts of O-acetylsalicylic acid with basic amino acids and glycine)

IT 62952-06-1P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(stabile active ingredient complex of salts of O-acetylsalicylic acid with basic amino acids and glycine)

IT 56-40-6, Glycine, biological studies 70-54-2, Lysine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stabile active ingredient complex of salts of O-acetylsalicylic acid with basic amino acids and glycine)

L17 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1291970 HCAPLUS
DOCUMENT NUMBER: 144:27608
TITLE: Combination of salts of o-acetyl salicylic acid and alpha-glucosidase inhibitors
INVENTOR(S): Ledwoch, Wolfram
PATENT ASSIGNEE(S): Bayer Healtcare AG, Germany
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005115404	A1	20051208	WO 2005-EP5224	20050513

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 102004025535 A1 20051222 DE 2004-102004025535 20040525
PRIORITY APPLN. INFO.: DE 2004-102004025535A 20040525

ABSTRACT:
The invention relates to a combination containing a salt of O-acetyl salicylic acid, a basic *amino acid* as constituent A, and an alpha-glucosidase inhibitor as constituent B for preventing cardiovascular diseases. The invention also relates to medicaments containing said combination, and to methods for producing the same.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IN *Ledwoch, Wolfram*

AB The invention relates to a combination containing a salt of O-acetyl salicylic acid, a basic *amino acid* as constituent A, and an alpha-glucosidase inhibitor as constituent B for preventing cardiovascular diseases. The invention also relates to medicaments. . .

ST *lysine* acetylsalicylate acarbose *particle size* cardiovascular disease glucosidase inhibitor

IT Brain, disease
Cardiovascular agents
Cardiovascular system, disease
Diabetes mellitus
Heart, disease
Hypertension
Particle size
Particle size distribution
(combination of salts of o-acetyl salicylic acid and alpha-glucosidase inhibitors)

IT *50-78-2*, o-Acetyl salicylic acid 199926-21-1 564444-68-4
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(combination of salts of o-acetyl salicylic acid and alpha-glucosidase inhibitors)

IT 37933-78-1P, L-*Lysine*-acetylsalicylate 870637-07-3P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(combination of salts of o-acetyl salicylic acid and alpha-glucosidase inhibitors)

L17 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:71842 HCAPLUS
DOCUMENT NUMBER: 136:123661
TITLE: Stable salts of o-acetylsalicylic acid with basic *amino acids*
INVENTOR(S): *Franckowiak, Gerhard*; *Appolt, Hubert*; *Leifker, Gregor*; *Wirges, Hans-Peter*; *Ledwoch, Wolfram*

PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany
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WO 2002005782	A2	20020124	WO 2001-EP7669	20010705
WO 2002005782	A3	20031002		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 10034802	A1	20020131	DE 2000-10034802	20000718
CA 2416288	A1	20030115	CA 2001-2416288	20010705
BR 2001012538	A	20030909	BR 2001-12538	20010705
HU 2003002053	A2	20030929	HU 2003-2053	20010705
EP 1365737	A2	20031203	EP 2001-956511	20010705
EP 1365737	B1	20050420		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004507463	T	20040311	JP 2002-511715	20010705
AU 2001278471	B2	20040722	AU 2001-278471	20010705
AT 293589	T	20050515	AT 2001-956511	20010705
ES 2241849	T3	20051101	ES 2001-956511	20010705
SK 286162	B6	20080407	SK 2003-67	20010705
US 20020091108	A1	20020711	US 2001-906497	20010716
US 6773724	B2	20040810		
IN 2003MN00014	A	20051021	IN 2003-MN14	20030102
NO 2003000222	A	20030116	NO 2003-222	20030116
MX 2003PA00510	A	20040420	MX 2003-PA510	20030117
ZA 2003000469	A	20040621	ZA 2003-469	20030117
KR 773658	B1	20071105	KR 2003-700713	20030117
HR 2003000108	B1	20061231	HR 2003-108	20030217
HK 1061811	A1	20060127	HK 2004-104934	20040707
US 20050009791	A1	20050113	US 2004-915652	20040809
AU 2004218728	A1	20041028	AU 2004-218728	20041013
AU 2004218728	B2	20061109		

PRIORITY APPLN. INFO.:		
DE 2000-10034802	A	20000718
AU 2001-278471	A3	20010705
WO 2001-EP7669	W	20010705
US 2001-906497	A3	20010716

ABSTRACT:
The invention relates to stable salts of o-acetylsalicylic acid with basic ***amino*** *acids*, to a method for producing them and to their use as drugs. Thus 9.9 kg acetylsalicylic acid were dissolved in 120 kg ethanol at 20-25°C; a solution of 9.0 kg *lysine* hydrate and 26.5 kg water were added while 30°C was not exceeded; crystallization was initiated with 50 g inoculation crystals, acetone, and cooling to 0°C. Crystals were filtered, centrifuged and dried below 40°C and 30 mbar. The yield was

89-94% ; residual moisture 0.10-0.15%.

TI Stable salts of o-acetylsalicylic acid with basic *amino acids*

IN *Franckowiak, Gerhard*; *Appolt, Hubert*; *Leifker, Gregor*; *Wirges, Hans-Peter*; *Ledwoch, Wolfram*

AB The invention relates to stable salts of o-acetylsalicylic acid with basic *amino acids*, to a method for producing them and to their use as drugs. Thus 9.9 kg acetylsalicylic acid were dissolved in 120 kg ethanol at 20-25°C; a solution of 9.0 kg *lysine* hydrate and 26.5 kg water were added while 30°C was not exceeded; crystallization was initiated with 50 g inoculation crystals,. . .

ST stable salt o acetylsalicylic basic *amino acid*; *lysine* acetylsalicylate stable salt basic *amino acid*

IT Purinoceptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(P2T, inhibitors; stable salts of o-acetylsalicylic acid with basic *amino acids*)

IT *Amino acids*, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(basic; stable salts of o-acetylsalicylic acid with basic *amino acids*)

IT Crystallization
(cocrystn.; stable salts of o-acetylsalicylic acid with basic *amino acids*)

IT Heart, disease
(infarction, therapeutic agents; stable salts of o-acetylsalicylic acid with basic *amino acids*)

IT Thrombin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; stable salts of o-acetylsalicylic acid with basic *amino acids*)

IT Muscle, disease
Pain
(myalgia, treatment of; stable salts of o-acetylsalicylic acid with basic *amino acids*)

IT Antiarthritics
Antimigraine agents
Calcium channel blockers
Crystallization
Nervous system agents
Particle size distribution
Stability
(stable salts of o-acetylsalicylic acid with basic *amino acids*)

IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(αIIbβ3, inhibitors; stable salts of o-acetylsalicylic acid with basic *amino acids*)

IT 62952-06-1P, *Lysine* acetylsalicylate
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cocrystn. with glycine; stable salts of o-acetylsalicylic acid with basic *amino acids*)

IT 56-40-6, Glycine, biological studies
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(cocrystn. with *lysine* acetylsalicylate; stable salts of

o-acetylsalicylic acid with basic *amino acids*)
IT 9002-05-5, Blood coagulation factor Xa
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; stable salts of o-acetylsalicylic acid with basic *amino acids*)
IT 67-64-1, Acetone, processes
RL: PEP (Physical, engineering or chemical process); PROC (Process)
(stable salts of o-acetylsalicylic acid with basic *amino acids*)
IT *50-78-2*, o-Acetylsalicylic acid 56-87-1, L-*Lysine*, reactions 70-54-2, *Lysine*
RL: RCT (Reactant); RACT (Reactant or reagent)
(stable salts of o-acetylsalicylic acid with basic *amino acids*)
IT *50-78-2DP*, o-Acetylsalicylic acid, basic *amino acid* salts of 37933-78-1P, *Lysine* acetylsalicylate
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(stable salts of o-acetylsalicylic acid with basic *amino acids*)
IT 70-26-8D, L-Ornithine, salt with o-acetylsalicylic acid 71-00-1D, L-Histidine, salt with o-acetylsalicylic acid 74-79-3D, L-*Arginine*, salt with o-acetylsalicylic acid 305-62-4D, salt with o-acetylsalicylic acid
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stable salts of o-acetylsalicylic acid with basic *amino acids*)

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(FILE 'HOME' ENTERED AT 03:57:55 ON 13 JUL 2008)

FILE 'CAPLUS' ENTERED AT 03:58:20 ON 13 JUL 2008
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L2 1 S DE-10034802.5/PN

FILE 'REGISTRY' ENTERED AT 04:31:04 ON 13 JUL 2008
E O-ACETYLSALICYLIC ACID/CN
L3 5 S E3-E7

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 04:32:36 ON 13 JUL 2008
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L5 1385 S (ACETYLSALICYCLIC OR 0-ACETYLSALICYCLIC) (W) ACID?
L6 184547 S L5 OR L4
L7 3449848 S LYSINE OR ARGININE OR AMINOBUTYRIC OR OMITHINE OR AMINO (W) A
L8 4660 S L6 AND L7
L9 2087871 S PARTICLE (S) SIZE OR DIAMETER OR RADIUS
L10 83 S L8 AND L9
L11 66 DUP REM L10 (17 DUPLICATES REMOVED)
L12 1385 S (ACETYLSALICYCLIC OR 0-ACETYLSALICYCLIC) (W) ACID?
L13 0 S L12 AND L11
L14 34 S L11 AND (AY<=2002 OR PY<=2002)
L15 10 S PARTICLE (S) (SIZE OR DIAMETER OR RADIUS) AND L14
L16 158 S (FRANCKOWIAK G? OR APPOLT H? OR LEIFKER G? OR WIRGES H? OR LE

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L17             3 S L11 AND L16
L18             0 S L11 AND L16D HIS

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                   275.27     336.16

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                   -10.40     -11.20

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